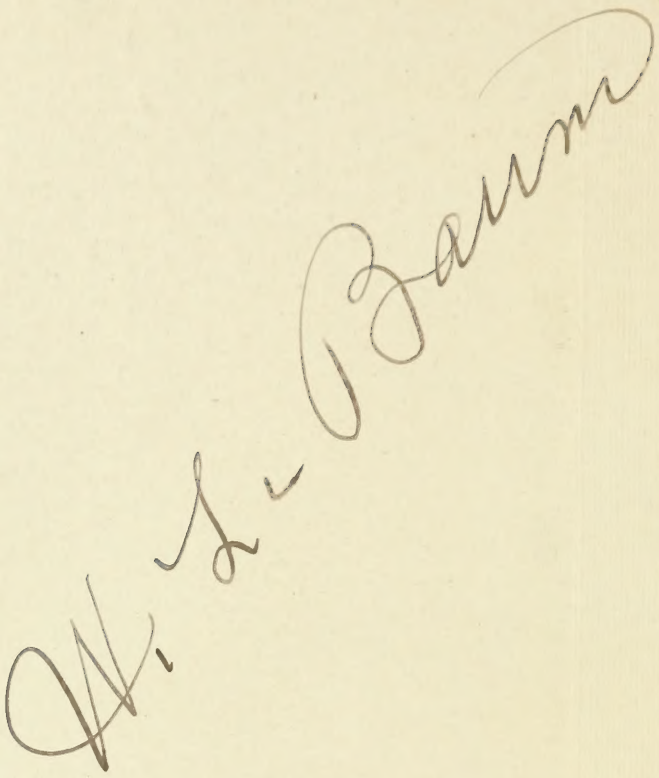


Digitized by the Internet Archive
in 2009 with funding from
University of Toronto

http://www.archive.org/details/transactions03chic

LIBRARY
APR 29 1946
UNIVERSITY OF TORONTO

TRANSACTIONS

OF THE

Chicago Pathological Society

FROM MAY, 1897, TO JUNE, 1899

* * *

VOLUME III

* * *

CHICAGO:
AMERICAN MEDICAL ASSOCIATION PRESS
1900

445792
1-5-46

RB
1
C45
v.3

PREFACE

It is probably needless to say that the Publication Committee does not assume responsibility for the different views and statements advanced by the authors of the various articles and reports in this volume.

The Committee desires to express its thanks to the publishers of the following journals for the free use of sundry cuts and plates for illustrations of articles already published by them, and reprinted here: *The New York Medical Journal, The Philadelphia Medical Journal, The Journal of Cutaneous and Genito-Urinary Diseases, The Journal of the American Medical Association,* and *Medicine.*

CONTENTS

List of Former Officers 5
List of Officers and Committees 1898-99 6
Necrological List 7
List of Members 9
The Central Nervous System 14
The Eye 68
The Ductless Glands 89
The Respiratory System 121
The Circulatory System 145
The Digestive System 175
The Genito-Urinary System 277
The Lymphatic System 345
The Skin 409
Miscellaneous 446

OFFICERS OF SOCIETY FROM 1882 TO 1899

YEAR.	PRESIDENT.	VICE-PRESIDENT.	SECRETARY.	TREASURER.
1882–83	H. M. Lyman.	H. Webster Jones.	Robt. S. Hall.	Robt. S. Hall.
1883–84	J. J. M. Angear.	D. R. Brower.	J. H. Tebbetts.	J. H. Tebbetts.
1884–85	J. J. M. Angear.	E. L. Holmes.	J. H. Tebbetts and H. N. Moyer.	H. N. Moyer.
1885–86	E. L. Holmes.	J. D. Skeer.	W. L. Copeland.	H. N. Moyer.
1886–87	Wm. E. Clarke.	C. J. Lewis.	W. L. Copeland.	Jos. Haven.
1887–88	I. N. Danforth.	A. H. Foster.	W. L. Copeland.	Jos. Haven.
1888–89	I. N. Danforth.	J. D. Skeer.	W. L. Copeland.	Jos. Haven.
1889–90	J. D. Skeer.	E. H. Root.	W. L. Copeland.	Jos. Haven.
1890–91	A. H. Foster.	E. H. Root.	W. L. Copeland.	J. M. Patton.
1891–92	E. H. Root.	C. D. Westcott.	E. S. Pettyjohn.	J. M. Patton.
1892–93	C. D. Westcott.	J. M. Patton.	E. S. Pettyjohn.	R. N. Hall.
1893–94	J. M. Patton.	H. N. Moyer.	J. M. Dodson.	R. N. Hall.
1894–95	R. N. Hall.	F. B. Earle.	G. H. Weaver.	Homer Thomas.
1895–96	W. Van Hook.	J. B. Herrick.	G. H. Weaver.	F. B. Earle.
1896–97	Jas. B. Herrick.	A. R. Edwards.	G. H. Weaver.	F. B. Earle.
1897–98	M. L. Harris.	Ludvig Hektoen.	G. H. Weaver.	F. B. Earle.
1898–99	Ludvig Hektoen.	Emil Ries.	G. H. Weaver.	F. B. Earle.

OFFICERS AND COMMITTEES

FOR 1898-99

PRESIDENT - - - - - - LUDVIG HEKTOEN

VICE-PRESIDENT - - - - - - - EMIL RIES

SECRETARY - - - - - - - GEORGE H. WEAVER

TREASURER - - - - - - - FRANK B. EARLE

BOARD OF CENSORS.

GEORGE HENRY CLEVELAND,

JOSEPH M. PATTON,

FRANKLIN C. WELLS.

PUBLICATION COMMITTEE.

LUDVIG HEKTOEN,

WELLER VAN HOOK,

GEORGE H. WEAVER.

NECROLOGICAL LIST.

Brown, I. W. ..... December 22, 1897
Skeer, J. D. ..... March 7, 1898
Clarke, William E. ..... March 22, 1898
Hamilton, John B. ..... December 24, 1898
Etheridge, James H. ..... February 9, 1899
Benson, John A. ..... March 9, 1899
Robinson, W. F. ..... May 12, 1899
Froelich, Hans.

LIST OF MEMBERS.

Angear, J. J. M., 482 W. Lake Street.
Angell, Katharine L., 3745 Indiana Avenue.
Auld, J. M., 714 W. Monroe Street.
Babcock, Robert H., 103 State Street.
Bacon, Charles S., 426 Centre Street.
Bartlett, R. H., 14 Loomis Street
Baum, W. L., 103 State Street.
Bausman, A. B., 580 W. Madison Street.
Beffel, J. M., 2400 Indiana Avenue.
Bevan, Arthur D., 100 State Street.
Billings, Frank, 100 State Street.
Bouffleur, A. I., 1178 Washington Boulevard.
Bridge, Norman, Los Angeles, Cal.
Brophy, T. W., 126 State Street.
Brower, D. R., 597 Jackson Boulevard.
Brown, Sanger, 757 Washington Boulevard.
Bryan, C. J., 1079 Washington Boulevard.
Burgess, A. J., Milwaukee, Wis.
Burroughs, W. M., 885 W. North Avenue.
Burwash, Henry J., 721 N. Hoyne Avenue.
Bush, Bertha, Rogers Park, Ill.
Campbell, Ralph R., 100 State Street.
Capps, J. A., 226 E. 53d Street.
Chandler, Ralph Milwaukee, Wis.
Chapman, C. F., 833 Washington Boulevard.
Chapman, George L., Alexian Brothers' Hospital.
Christopher, W. S., 408 Centre Street.
Class, W. J., 1301 Belmont Avenue.
Clausen, James J., Kansas City, Mo.
Cleveland, George H., 951 W. Harrison Street.
Coates, W. E., 655 W. 12th Street.
Colburn, J. E., 34 Washington Street.
Cook, E. P., 284 Lincoln Avenue.
Cooke, Jean M., 1609 Diversey Boulevard.
Coolidge, F. S., 103 State Street.
Copeland, W. L., 918 Warren Avenue.
Corwin, A. M., 301 Ashland Boulevard.
Cotton, A. C., 677 Jackson Boulevard.
Coulter, J. W., 103 State Street.
Croftan, A C., 103 State Street.
Dal, John W., 499 N. Robey Street.
Danforth, I. N., 758 W. Adams Street.

Davis, Thomas A., 987 Jackson Boulevard.
Dewey, F. J., 302 S. Oakley Avenue.
Diamond, I. B, 587 S. Halsted Street.
Dickerman, Edward T., 103 State Street.
Dodson, John M., 568 Washington Boulevard.
Doepfner, Karl, 581 Orchard Street.
Doherty, David J., 143 North Avenue.
Donaldson, H., University of Chicago.
Dudley, E. C., 1617 Indiana Avenue.
Earle, F. B., 903 W. Monroe Street.
Eckley, W. T., 385 Washington Boulevard.
Edwards, A. R., 2818 Indiana Avenue.
Eisendrath, D. N., 3125 Michigan Avenue.
Evans, W. A., 103 State Street.
Favill, H. B., 100 State Street.
Fisher, John, 364 La Salle Avenue.
Fitch, C. M., 645 W. Monroe Street.
Fitch, W. M., 645 W. Monroe Street
Foster, A. H., 779 W. Monroe Street.
Friend, E., 70 State Street.
Friend, S., Milwaukee, Wis.
Fütterer Gustav, 716 Fullerton Avenue.
Gavin, E. F., Waukegan, Ill.
Gehrmann, A., 103 State Street.
Gentles, H. W., 210 E. 51st Street.
Gill, James C., 833 Warren Avenue.
Graham, D. W., 672 W. Monroe Street.
Grinker J., 952 Milwaukee Avenue.
Grim, U. J., 247 W. Madison Street.
Gunn, Janet, 70 State Street.
Hall, R. N., 339 Warren Avenue.
Hamill, Edwin, 812 Warren Avenue.
Hamilton, Alice, Hull House.
Hammon, G. M., 683 W. Adams Street.
Hanson, Z. P., 304 Washington Boulevard.
Harlan A., Masonic Temple.
Harris, M. L., 100 State Street.
Hartman, F. S., 568 Congress Street.
Harvey, R. H., 2100 Calumet Avenue.
Heineck, A., 872 Trumbull Avenue.
Hektoen, Ludvig, Rush Medical College.
Henkel, F. W. E., 538 Ashland Boulevard.
Henrotin, Fernand, 353 La Salle Avenue.
Herb, Isabella C., 51 Lincoln Avenue.
Herrick, James B., 751 Warren Avenue.
Herzog, Maximilian, 174 E. Chicago Avenue.
Hessert, William, 25 Roslyn Place.
Hoadley, A. E., 683 Washington Boulevard.
Hodges, F. J., Ashland, Wis.

Hollinger, J., 103 Randolph Street.
Holmes, E. L., 31 Washington Street.
Hook, E. I., 1522 N. Rockwell Street.
Ingals, E. F., 34 Washington Street.
Jay, Frank W., 2510 Indiana Avenue.
Johnson, Frank S., 2521 Prairie Avenue.
Jordan, E. A., University of Chicago.
King, Herbert M., Grand Rapids, Mich.
Klebs, Edwin, 52 Walton Place.
Klebs, Arnold, 600 State Street.
Kerr, N., 295 La Salle Avenue.
Kohn, Alfred D., 3340 Michigan Avenue.
Latham, V. A., Rogers Park, Ill.
Leach, W. D., 1105 W. North Avenue.
Leahy, M. M., 6301 Wentworth Avenue.
Leahy, Sarah J. M., 6301 Wentworth Avenue.
Lee, Edward H., 100 State Street.
Lee, Frances H., 3738 S. Halsted Street.
Le Count, E. R., 398 Marshfield Avenue.
Lemke, A. F., 103 State Street.
Lewis, C. J., 733 Carroll Avenue.
Lewis, H. F., 4426 Lake Avenue.
Linnell, B. M., 197 Clybourn Avenue.
Loeb, J., University of Chicago.
Loomis, E. B., 145 S. Robey Street.
Luken, M. H., 587 W. North Avenue.
Lumley, R., 1074 N. California Avenue.
Lyman, Henry M., 200 Ashland Boulevard.
Marshall, F. D., 679 W. Adams Street.
Maywit, M., Belmont Avenue and Halsted Street.
MacMartin, D. R., 77 Jackson Street.
McArthur, L. L., 100 State Street.
McCullum, J. L., 626 W. Lake Street.
McCullough, J. R., 37 Park Avenue.
McDill, John R., Milwaukee, Wis.
McIntyre, C. J., 834 Grand Avenue.
Meling, N. C., 952 Armitage Avenue.
Mergler, Marie J., 100 State Street.
Methews, Samuel A., 118 E. 53d Street.
Meyers, Adolph, Worcester, Mass.
Miller, Truman W., 1071 N. Clark Street.
Mitchell, Louis J., 498 Adams Street.
Misick, O. S., 445 North Avenue.
Montgomery, Frank W., 100 State Street.
Moorehead, E. L., 474 Ashland Boulevard.
Morris, John L., Clark Street and North Avenue.
Moyer, Harold N., 103 State Street.
Mueller, George, 1063 Milwaukee Avenue.
Murphy, J. B., 103 State Street.

Newman, H. P., 103 State Street.
Newton, G. W., 878 W. Adams Street.
Noel, E. P., 577 W. Congress Street.
Ochsner, A. J., 710 Sedgwick Street.
Ochsner, E. H., 710 Sedgwick Street.
Olney, T. A., 1038 Jackson Boulevard.
O'Neill, J. W., 1382 N. Clark Street.
O'Shea, D., 470 Ashland Boulevard.
Parker, Charles A., 776 W. Lake Street.
Patrick, Hugh T., 34 Washington Street.
Peterson, R., 103 State Street.
Pettyjohn, Elmore, Alma, Mich.
Plummer, S. C., 4304 Lake Avenue.
Preble, R. B., 590 Dearborn Avenue.
Prendergast, Joseph, Lake Street and Kedzie Avenue.
Pfeifer, John P., 1214 Milwaukee Avenue.
Price, O. J., 538 W. Adams Street.
Pritzker, L. J., 239 W. Division Street.
Pusey, W. A., 103 State Street.
Regent, M. N., 564 S. Halsted Street.
Rhodes, John Edwin, 34 Washington Street.
Richards, Annette S., 821 Warren Avenue.
Ricketts, H. T., 100 State Street.
Ries, Emil, 100 State Street.
Rittenhouse, William, 975 Warren Avenue.
Robison, John A., 297 Ashland Boulevard.
Root, Eliza H., 489 W. Monroe Street.
Ross, J. W., 925 Warren Avenue.
Rumpf, W. H., 100 State Street.
Ryan L., 1285 W. Van Buren Street.
Salisbury, J. H., 982 W. Adams Street.
Sandberg, Karl F., 622 N. Hoyne Avenue.
Schaeffer, F. C., 582 Washington Boulevard.
Schroeder, William E., 4323 Prairie Avenue.
Senn, E. J., 532 Dearborn Avenue.
Seville, F. F., 1620 W. Madison Street.
Simmons, George H., 61 Market Street.
Sippy, B. W., 143 Oakwood Boulevard.
Shaw, D. Lee, 707 Jackson Boulevard.
Slaymaker, S. R., 1318 Washington Boulevard.
Somers, G. H., 514 Jackson Boulevard.
Steele, D. A. K., 103 State Street.
Stehman, H. B., Presbyterian Hospital.
Stevenson, Alex. F., Jr., Presbyterian Hospital.
Strong, A. B., 533 W. Monroe Street.
Tebbetts, J. H., Hollister, Cal.
Test, Annabel Cleveland, 4401 Indiana Avenue.
Thomas, H. M., 31 Washington Street.
Thometz, John L., 999 W. 12th Street.

Tice, F., Dunning, Ill.
Turck, F. B., 555 Dearborn Avenue.
Twining, S. D., 210 Grand Avenue.
Van Hook, Weller, 4043 Grand Boulevard.
Van Hoosen, Bertha, 489, 42d Street.
Wagner, Carl, 74 Lincoln Avenue.
Waite, Lucy, 98 Loomis Street.
Watkins, T. J., 93, 18th Street.
Walls, Frank X., 103 State Street.
Waugh, William L., 103 State Street.
Weaver, George H., 535 Washington Boulevard.
Weber, Samuel L., 100 State Street.
Wells, Franklin C., 883 W. Monroe Street.
Wescott, C. D., 31 Washington Street.
Wesener, J. A., 103 State Street.
Wilder, William H., 103 State Street.
Willson, Charles G., Milwaukee, Wis.
Williams, John C., 169 Webster Avenue.
Wing, Elbert, 55, 33d Street.
Woley, H. P., 43d Street and Grand Boulevard.
Worthington, H. C., Oak Park, Ill.
Zeit, Robert F., 4016 Vincennes Avenue.

THE CENTRAL NERVOUS SYSTEM

CYSTICERCUS CELLULOSAE OF BRAIN AND SPINAL CORD.

I. B. DIAMOND.

The relation between the common bladder-worm of the pig, or *cysticercus cellulosae,* and the hook-bearing tapeworm that infests the intestines of man, known as tenia solium, was not recognized until 1853, when Küchenmeister first called attention to the resemblance of the bladder-worm head and the head of the tenia solium.[1] His observations were soon corroborated, mainly on experimental grounds, by Leuckart,[2] Haubner, Van Beneden and many others[3]—that the eggs of tenia solium, when introduced into the stomach of the pig, by feeding pigs with ripe segments, develop into the familiar bladder-worm (measly pork)—and that the latter is the larval form of the above tenia. Furthermore, the life cycle of this parasite is completed by the metamorphosis of the bladder-worm into the adult tapeworm, when the bladder-worm is taken into the stomach of man and in a few of the lower animals. The knowledge of its life history is of considerable importance, since the larval stage of this worm, as is well known, is also capable of developing in man, and at times producing serious results, especially when the cysticerci are situated in the brain, eye and heart muscle.

Leuckart divides the life history of the tapeworm into five stages: 1, the six-hooked embryo; 2, the bladder-worm or cysticercus cellulosæ; 3, the tapeworm head without joints (scolex); 4, the proper chain-like form

(strobila); and 5, finally, the isolated sexual animal, segment or proglottis. Practically two stages only are considered, the larval and the adult. Starting with the adult tapeworm in the intestine of man, the infection with the larval form and its mode of development in man is briefly as follows: The ripe eggs or six-hooked embryos escape from the uterus of the segment and pass out with the excreta, or segments may break loose from the worm and then pass out with the excreta. A person may soil his hands with the eggs by handling the segments, and afterward swallowing them, or they may gain access through contaminated water. Self-infection may also take place. The segments may be carried into the stomach by reverse peristalsis. On arriving in the stomach, the embryos bore their way through the walls of the stomach by means of the six little hooks and wander to the muscles, or penetrate a blood-vessel, and may then be carried to various organs of the body. The embryo loses its hook when it come to rest, increases in size and develops into a round bladder-worm or cysticercus. During its development it may become encapsulated by connective tissue of the host, as a result of reactive inflammation. A fully developed bladder-worm consists of the future tapeworm head (scolex) with its suckers and row of hooks. The head is formed in an invagination of the cyst wall. The whole process of formation is estimated as from ten to eighteen weeks. The bladder-worm is capable of living for years, but as a rule it undergoes calcareous degeneration when the cyst becomes quite old, resembling on examination a cheesy tubercle.

As to the frequency of cysticercus cellulosæ in America—it must indeed be a rare disease. Stiles,[4] who is an authority on the subject, calls attention to the rarity of tenia solium and its larval stage (cysticercus cellulosæ) in America, not only in man, but also in the hog. I have collected only eight cases from American literature. The first case seems to have been reported by

Schilling[5] of New York, in 1857. The patient was a German woman, 31 years of age. She had epilepsy for a number of years, and other nervous symptoms. On post-mortem examination, numerous cysticerci were found in the brain, and several in the heart muscle. In five cases the parasite was present in the eye. Reynolds[6] of Louisville reported one case in 1874; Kipp[7] of Newark, N. J., one in 1876, and C. S. Turnbull[8] of Philadelphia a case in 1879. The other two cases quoted by him were reported, one by Calhoun of Atlanta, Ga., in 1878, and the other by Morton (Philadelphia?), in 1870. Osler[9] mentions a case in his "Practice of Medicine" which came under his observation; the cysticerci were present in the subcutaneous tissue. Recently a case was reported by Cattell;[10] the patient was thought to have died of hydrophobia—a few cysticerci were found in the brain.

The case now to be reported was that of a married woman, white, aged 34, a native of Germany, residing in Cook County, Illinois, for fourteen years, and admitted to the Cook County Hospital, Chicago, on Oct. 22, 1898, in the service of Dr. Blouke. At the time of admission the patient was unconscious, and the following history was obtained from the relatives: Menses began at 16; regular, but accompanied by more or less dizziness; was married at age of 21, but never became pregnant. She always had "fits" at the time of the monthly sickness, and they have become more severe during the last ten years. These attacks could always be foretold and the patient would remove her clothing preparatory to the attack, which would last for five to ten minutes. After the convulsion she would remain in bed for about eight days. On October 20 she became frightened, and recognizing the oncoming of a convulsion, went to bed. Afterward the convulsions continued quite constantly at intervals of half an hour, and during that time she had taken no food or drink. The eyelids were partly closed, pupils contracted, supraorbital reflex absent. There was labial

stertor, lips and tongue dry. At intervals there were marked spasms, but no screaming and no vomiting. On catheterizing a small quantity of urine was obtained, which showed abundant albumin, but no sugar; a few hyaline casts. The convulsions continued until death, which occurred Oct. 23, 1898. The clinical diagnosis was uremia. The post-mortem examination was made by Prof. L. Hektoen, the following day, and he kindly furnished me the following notes, with the above clinical history:

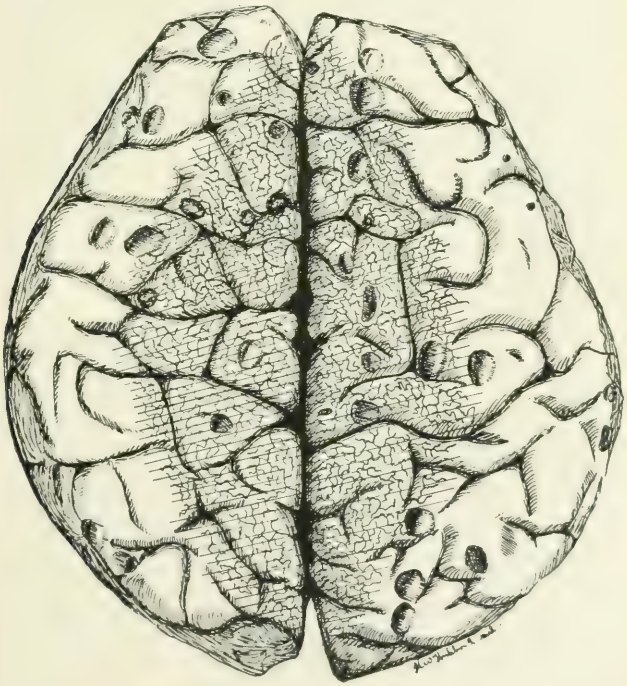


Figure 1.

Anatomic diagnosis.—Cysticercus cellulosæ of brain and spinal cord; adhesive pleuritis; bronchitis; bronchopneumonia; menstruation; lymphatic constitution (persistent thymus, enlarged intestinal follicles); parovarian cyst.

The general nourishment is good; rigor prominent; lividity posteriorly. The abdominal cavity is empty, lining smooth;

pleural and pericardial cavities are empty; there are some fibrous adhesions over the left upper lobe. Tongue, pharynx and esophagus normal; thyroid gland of ordinary size; thymus gland present in the form of a mass of fat tissue, which corresponds to the thymus in shape and size and which contains quite extensive islands of glandular tissue. The lungs float and crepitate. In the right lower lobe is a small grayish-red area which is solid and granular, and around which the bronchi contains pus. The peribronchial lymph-glands are normal. The heart is normal as to its internal lining. The flesh is rather flabby and loose; weight 300 grams. The coronary vessels and aorta are smooth. The spleen weighs 150 grams, capsule smooth, cut surface red, rather soft. The kidneys weigh 300 grams, capsule free except over small areas, color red, cut surface moist, cortical markings distinct; in the center of one pyramid is a whitish area as large as a grain of wheat. The liver weighs 1375 grams, surface smooth, yellowish red; consistence normal, lobular markings rather indistinct. The biliary apparatus is normal. The pancreas, stomach, small and large intestine are normal, except that in the lower part of the ilium the Peyer's patches show rather prominent follicles. The bladder and urethra show no changes. The uterus presents a virgin os; in the cavity is a loose mass of blood. In the center of the right ovary is a mass of clotted blood, 2 cm. in diameter, red, and in places adherent to the smooth walls of the cavity in which it lies. In the right appendage is a parovarian cyst as large as a hickory nut. The serous surfaces of the pelvic organs are smooth. The scalp and skull show no changes. The dura is adherent to the pia at several small areas, on account of the presence of rather small cystic bodies between the two membranes, the bodies being lightly adherent to both.

The brain weighs 1250 grams. (Fig. 1.) Scattered over the entire surface are smaller and larger globular cysts with clear contents and thin walls, as well as shrunken, yellowish, irregular, granular, smaller masses. These cysts and masses are imbedded in the cerebral cortex, having made for themselves distinct depressions, clothed with pia, in which they lie loosely or slightly adherent. The largest of these cysts measure 2 cm. in diameter. There are perhaps ten or fifteen such masses scattered over the right occipital lobe. They also occur on the internal surface of the two hemispheres. The subdural space of the spine contains several flat, grayish, oval or rounded masses, similar to those on the cerebral surface. These are present in considerable numbers throughout the entire spinal subdural space.

Additional Note.—There are six granular bodies attached to the inner surface of the dura. The adhesion of the dura to the pia is seen especially over the parietal

and occipital lobes, and to a slight extent over the left frontal lobe. The fissures of the brain are obliterated by adhesions of the arachnoid and pia, which are thickened, opaque and grayish. The blood-vessels are dis-

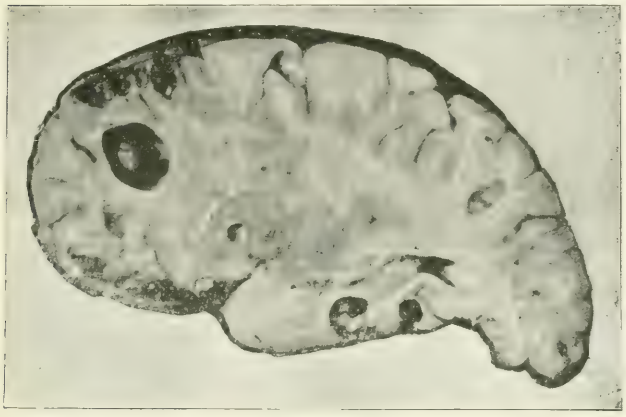


Figure 2.

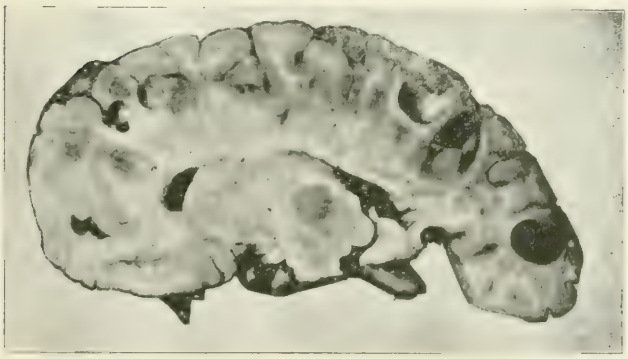


Figure 3.

Figures 2 and 3 are brain sections showing cysts in cortex and numerous calcareous bodies in basal ganglia.

tended with dark blood. The surface of the convolutions is somewhat flattened. The smaller cysts are usually situated in the fissures and sulci, while the larger ones,

which have made deep depressions into the cortex, may extend throughout its entire thickness. On puncturing one of the medium-sized cysts, the contents is easily removed, consisting of an elongated, curled-up, hard body and enclosed by a yellowish, delicate membrane. The smaller, irregular, grayish masses, on section, are filled with a cheesy or calcareous substance, surrounded by a thick wall of connective tissue. There are seven cysts over the right superior frontal convolution, from 1 to 2 cm. in diameter. Several smaller masses are scattered over the right middle and inferior frontal convolutions. Two cysts 2 cm. in diameter are situated on the right middle frontal convolutions, four in the left precentral fissure, and several smaller masses in the left inferior frontal convolutions. They are not so numerous over the parietal lobes, but are quite large and situated near the fissure of Rolando, more pronounced on the right. Several bodies varying in size from a pea to 2 cm. in diameter are situated in the fissure of Sylvius on both sides. The temporo-sphenoidal lobes are less involved, the bodies are present especially over the inferior convolutions. A number of the cysts are scattered over the base of the brain. One body, 2 cm. in diameter, is situated to the right of the optic nerve, making a deep depression in the frontal lobe, and another behind it, below the optic tract, surrounded by adhesions. (Figs. 2, 3.) Sections through the interior of the brain expose to view several dozens of these cysts. They are most numerous in the cerebral cortex of the frontal and occipital lobes, and especially of the right hemisphere. They vary in size from that of a pea to a large cherry. The smaller masses are calcified and surrounded by a connective-tissue capsule. These smaller masses are also scattered throughout the white substance, in the basal ganglia, optic thalami and corpus striatum. A cyst the size of a small cherry is situated in the posterior and lower portion of the corpus callosum,

making an excavation for itself. Another, which is long and thin-walled, is in the right frontal lobe.

Spinal cord.—The dura is adherent at many points to the pia. Over the anterior surface of subdural space are scattered a number of flat, calcified, oval masses, more numerous in the dorsal and lumbar regions, imbedded in

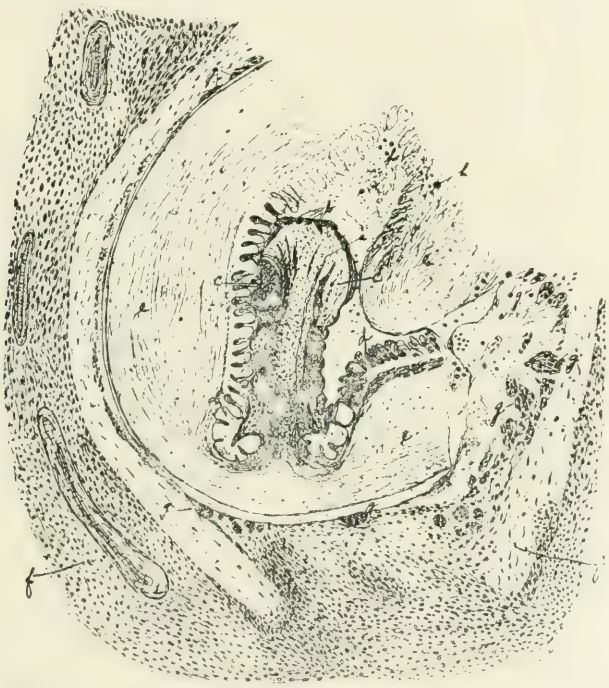


Figure 4.—*a*, Tapeworm head; *b*, hooks; *c*, suckers; *d*, folds; *e*, cyst wall; *f*, capsule of granulation tissue; *g*, giant cells; *h*, calcareous bodies.

the pia, averaging 1 cm. in diameter. Those in the cervical region are small, somewhat larger than a pin's head. The posterior subdural space contains but a few of these masses, in the lumbar and dorsal regions.

Histologic examination.—For microscopic study, several cysts were removed from the brain, dura and spinal cord, imbedded in celloidin, and sections stained with

hematoxylin and eosin, Van Gieson, etc. A globular cyst containing a somewhat elongated calcareous body was punctured, laid open, flattened between two slides, which on examination with the low power revealed several rows of hooks and the suckers of a tapeworm head.

Cysts of dura (Fig. 4).—In the center of a longitudinal section an elongated body is seen, resembling a tapeworm head. Several hooks can be made out, and beneath, on either side, are two suckers. The head arises by a kind of neck or base from the cyst wall, by which it is surrounded. The inner border of this wall is thrown into numerous folds, traceable to the sides of the head. The cyst wall is greatly thickened and has undergone calcareous degeneration. From the appearance and position of the head, it would seem, according to Leuckart,[11] that the head has protruded from its original position, and pushed itself into the cylindric body. The inner surfaces, formerly external, come in close contact, uniting and forming a solid mass, while the cuticular coat, mentioned above as folds, lies external. Scattered everywhere throughout the body and cyst wall are numerous calcareous bodies of various sizes, resembling ova and staining deeply with hematoxylin. The whole cyst is enclosed by a connective-tissue capsule, composed largely of granulation tissue. Lying next to the cyst wall, the tissue is fully formed and mostly fibrous in structure, throughout which are scattered a large number of variously shaped giant cells. Besides the giant cells, the cells of the tissue are of two kinds: 1, small cells with deeply staining nuclei; and, 2, larger cells with vesicular nuclei, which stain lightly and in shape are either oval, spindle-shaped or oblong. Here and there through the tissue are seen the remains of obliterated larger and smaller blood-vessels. (Fig. 5.) The giants cells are, as mentioned, situated in the fully-formed fibrous connective tissue, and are most numerous next to the cyst wall. Others lie within the cysts, or

partly within by shoots of their cytoplasm. They vary in size and shape. Some are round or oval, others spindle-shaped and irregularly oblong. Many of the giant cells have quite a large number of nuclei, which stain deeply, are rich in chromatin, oval or spindle-shaped, and fill completely by their numbers the protoplasmic masses. In others the nuclei are less in number, stain poorly, are swollen, elongated and vesicular, and are irregularly scattered or concentrically arranged around the periphery. A deeply-stained nucleus may, however, be seen among them. In the last-named cells there are evidences

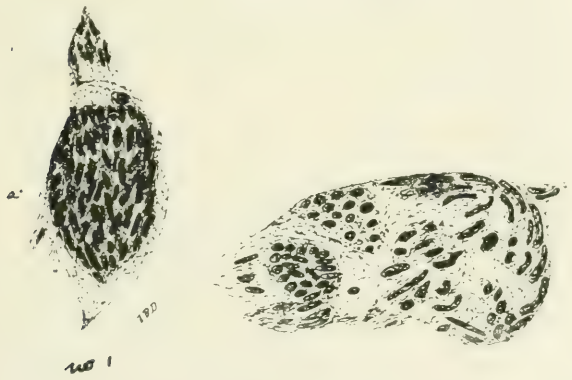


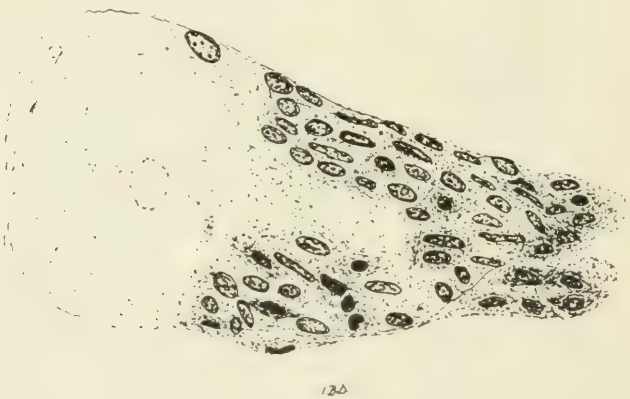
Figure 5.

No. 1.—Giant cell, nuclei rich in chromatin and arranged to long axis of the cell. 1-12 oil immersion; hematoxylin and eosin.

No. 2.—A giant cell, with irregular-shaped nuclei collected in masses and evidently separating. 1-12 oil-immersion; hematoxylin and eosin.

of degeneration. The protoplasm is occasionally vacuolated and stains faintly with eosin. The degeneration is more marked in those cells lying within the cysts. There are giant cells apparently separated into protoplasmic masses or in the act of fusion. Many of the smaller-celled masses lying in the connective tissue, having deeply and lightly stained nuclei, resemble remains of giant cells, their protoplasm blending with the surrounding tissue. It would here be proper to state, since Hektoen[12]

has called our attention to the fate of the giant cells in healing tuberculous tissue, that they undergo progressive changes and separate into small living cells, and which he further demonstrated experimentally in the rabbit's eye.[13] It would therefore suggest from the general appearance and arrangement of the giant cells here described, that the majority are undergoing a like fate. This statement I believe is justifiable for the reason that the giant cells are, as a rule, well preserved, while the surrounding tissue is quite old; that their nuclei are rich in chromatin, become elongated and arrange themselves to the long axis of the cells, and that small protoplasmic masses seem to separate from the giant cells and become enclosed by the surrounding tissue.



No. 3.—A degenerated giant cell; nuclei swollen, among which are seen deeply-stained nuclei. Hematoxylin and eosin.

Transverse sections through a small cyst imbedded in the cerebral cortex and lying partly within a sulcus surrounded by pia, show the cyst completely degenerated. It is filled by a calcareous or cheesy-like substance, and encapsulated by a thick wall of fibrous tissue. Lying next to the cyst and embedded in the fibrous tissue are a small number of giant cells. Surrounding the capsule is a zone of granulation tissue, composed largely of small

round, deeply-stained cells, throughout which are seen various-sized capillaries, with somewhat thickened walls. This tissue, which is identical with the pia, is adherent to the cortex. The change in the cortex is that also of a reactive inflammation. It is extensively infiltrated with small round cells, while next to the pia it is distinctly fibrillar. The blood-vessels are congested, and their walls thickened and infiltrated with small round cells. The lumen in others is obliterated. The changes of the ganglion cells are those due to pressure. Some have lost their outline, the nerve processes have disappeared and their nuclei are swollen. In others proliferative changes are present, the nuclei stain deeply, and there may be more than one nucleus in a cell.

An examination of sections of another somewhat larger, globular cyst, with clear contents and also taken from the cerebral surface, shows no head or hooks. The center is divided into several smaller cysts, throughout which are scattered a number of calcareous bodies. The cyst wall consists of two layers, an outer cellular attached to the capsule, and an inner, fibrillar, delicate-like membrane.

Compound cysts,[14] like this one, have been reported quite frequently. They usually are irregular in shape, and heads are but rarely found—C. racemosus of Zenker, who first described them.

Spinal cord.—The central canal is obliterated, and around its position are scattered a number of round, deeply-stained cells. The blood-vessels of the gray and white matter are distended with blood, and their walls are thickened. The ganglion cells as well as the nerve-fibers of the white substance are normal. The smaller and larger blood-vessels of the pia mater are congested, more like thrombosed. Around many of the blood-vessels are collections of small, round cells. To one side of the pia is seen one of the oval flat masses. It is dense

and homogeneous, and throughout are scattered a number of nuclei.

Sections of the thymus show, on microscopic examination, a number of follicles imbedded in fat tissue. It is composed of closely-packed, deeply-staining cells. Many blood-vessels are scattered throughout these islands, and in the fat tissue. They are greatly distended with blood and contain quite a large proportion of leucocytes. The larger vessels in the fat tissue are thickened and some evidently contain thrombi, which are organizing.

Summary.—It is evident from the foregoing that we are here dealing with a long-standing infection from the larva of tenia solium. While it is impossible to say how long the cysticerci have been present in the brain, we may infer from the clinical history, as well as from the examination of the cysticerci, that it is of at least twelve years' duration, if not longer. Cases have been reported where the bladder-worm has caused cerebral disturbance for fifteen years. Marchand reported a case of over ten years' standing. In what manner the ova gained entrance in this case, I am unable to say. There is no history of tapeworm. I question, however, whether the infection is of American origin, for the reason that the convulsions began when she was 16, four years before she came to this country. Besides, the few cases reported were mostly in Germans.

Furthermore, Stiles states[15] that he has yet to see a "pork" tapeworm of American origin. He believes those cases reported in the literature as tenia solium are really, from the general descriptions, the "beef" tapeworm—tenia saginata.

I believe we may safely conclude that the convulsions are the result of the constant pressure and irritation of the cysticerci on the brain, and which (finally) caused death; that the cysticerci acting as foreign bodies produced a chronic reactive inflammation of the brain and meninges; and, finally, that the giant-cells formed

around these bodies participate in the formation of the capsules.

May 8, 1899.

BIBLIOGRAPHY.

1. Küchenmeister: Ueber Cestoden in Allgemeinen, pp. 78, 89, 1853.
2. Leuckart: Parasites of Man.
3. See Leuckart.
4. Stiles: Notes on Parasites On the Rarity of Tenia Solium in North America, Vet. Mag., 1895. pp. 194-203.
5. Schilling, E.: N. Y. Jour. of Med., 1857.
6. Reynolds, D. S.: Am. Pract., June, 1874.
7. Kipp, C. J.: Internat. Ophth. Congress, 1876.
8. Turnbull: Transactions Medical Society of Penn., Phila., 1879, part ii, p. 674.
9. Osler: Practice of Medicine.
10. Cattell: Phila. Med. Jour., Jan. 14, 1899.
11. Leuckart: Development of Cestodes, p. 354.
12. Hektoen: Jour. of Exp. Med., vol. iii, No. 1, 1898.
13. Hektoen: Ibid., vol. iii, No. 6, 1898.
14. Marchand: Ein Fall von sogenanten "Cysticeus racemosus," des Gehirns, Virchow's Arch., B. lxxv.
15. Stiles, Vet. Mag.,1895, and Bulletin No. 19, U. S. Dept. of Agri. Bureau of Animal Industry.

SOME OBSERVATIONS UPON THE MOTOR SPINAL GANGLION CELL.

MARTIN H. FISCHER.

It is the object of this paper to set forth some of the results obtained from the study of the motor ganglion cell. The material employed was the human spinal cord, and the spinal cord of the white rat and dog.

Upon the use of methylene blue, thionin, bismarck brown, safranin O, fuchsin, hematoxylin, carmine, eosin, acid fuchsin, orcein, and their combinations, I have found that the spongioplasm of the cell body has a honeycomb structure. It is seen as a network with nodal thickenings. It is amphophilic. The claim of Ewing that it is visible in specimens stained by methylene blue is supported by my observations, and I have further been able to demonstrate it in sections stained with safranin O, or fuchsin. No evidence of the fibrillar structure described by Heiman, Flemming, Golgi,

Lugaro, Dogiel, Nissl, Becker, and others has been found.

Nissl has divided cells into those deeply stained—the pyknomorphous, those lightly stained—the apyknomorphous—and those occupying an intermediate position—the parapyknomorphous. Experimental study has shown that the three conditions are due entirely to technical processes employed.

Much significance has been attached to the appearance of the granule masses in the cell body which constitute the so-called Nissl bodies. The existence of these in the living cell is maintained by Flemming, Marinesco, Dogiel, Lenhossèk, Heiman, and Arnold. Held considers them to be artifacts due to the action of acid fixing agents. Rudzicka also believes them to be artifacts, as he has never been able to find them in unstained cells.

My investigation of cells teased in normal salt solution, cells soaked in iodo-potassium iodide solution according to Arnold's method, and of unstained sections hardened in corrosive sublimate, alcohol, formalin, Müller's fluid, 2 per cent. potassium bichromate, a mixture of alcohol and formalin, potassium bichromate and formalin, and after treatment with Weigert's mordant, shows the protoplasm to be generally granular, but no Nissl bodies are demonstrable in it.

My observation under the microscope of staining by methylene blue according to Nissl's method shows that at no time before the use of the differentiating alcohol does the protoplasm show anything save a general granular structure, with the densest aggregation of granules in the perinuclear region. No traces of Nissl bodies are visible.

When alcohol is allowed to act upon the stained cell, an unequal lightening of the protoplasm occurs, and darker areas are seen scattered through it which correspond to the Nissl bodies which appear later. Upon the

further use of alcohol the characteristic appearance of the Nissl bodies is obtained. A prolonged action of the alcohol causes the section to fade completely, and the structure of the unstained cell reappears. Upon restaining the cell, the arrangement of the Nissl bodies is by no means always found to be the same as that first observed. This latter fact I consider in itself a conclusive argument for the statement that the Nissl bodies are not structures which actually exist ready formed in the cell, but result from the action of certain substances upon its protoplasm.

Upon the observation of a series of stained specimens, these facts were noted in regard to the appearance of the Nissl bodies.

1. They are not seen when the cells are stained by hematoxylin or carmine.

2. They are seen in the hematoxylin specimens when these are differentiated in acid alcohol.

3. They are not seen in specimens stained with eosin, orcein, or acid fuchsin.

4. They are seen in sections stained in methylene blue, thionin, safranin O, bismarck brown, and fuchsin, but only after these have been differentiated.

Thus we are compelled to recognize the fact, that the Nissl bodies are demonstrable by no methods except those in which a differentiating agent is used. I believe the appearance of the Nissl bodies to depend upon certain physical conditions. Any barrier which prevents the action of the differentiating agent upon the stained cell, may give rise to such artifacts as the Nissl bodies. As an explanation of what might constitute such barriers, the following is offered.

Firstly. It has been noted that in the unstained cell the protoplasm is most granular just surrounding the nucleus. Now it so happens that the largest, deepest, and most tenaciously stained Nissl bodies also occur in the perniculear region. Galeotti and A. Fischer have al-

ready called attention to the fact that granules, closely arranged, absorb coloring matter much more intensely, and destain with much greater difficulty than do loosely arranged parts. Such conditions are present in the case under our consideration. In staining, the color is deposited between the granules, but when the differentiating agent is employed, all parts of the cell protoplasm do not destain with equal rapidity. Those portions in which the granules are most closely arranged offer a barrier to the action of the differentiating fluid, and hence non-destained parts result. These portions of the cell protoplasm which have been able to resist the action of the differentiating agent constitute the Nissl bodies. Why the Nissl bodies should at one time occupy a certain position in the cell, and then show after destaining and restaining, another arrangement is a question which I do not attempt to answer.

Secondly. When methylene blue specimens are counterstained by eosin or acid fuchsin, it is seen under favorable illuminating conditions, that delicate red stained edges outline the Nissl bodies, which are identical in appearance with the reticulum of the cell body. This would go to show that the cellular reticulum serves as an effective protection against the action of the differentiating medium. Coupling this with the observation that the Nissl bodies when entirely destained do not show the same arrangement when restained, leads me to attribute the occurrence of a Nissl body in a certain position in the cell, entirely to chance. In brief, the Nissl bodies represent artifacts which under constant conditions give constant appearances.

It is now the generally accepted view that the nerve elements are independent structures. (Lenhossèk, Golgi, Ramon y Cajal, etc.) Gerlach, by the use of gold chlorid, Held working with Golgi's method, Dogiel by the intravenous injection of methylene blue, Bethe with molybdic acid toluidin blue, and Rudzicka using toluidin

blue, maintain, however, that the independence of the cell elements is by no means a settled question.

My observations to determine the relations of the nerve cells to each other, and to the other structures of the spinal cord, have brought out some points which are at variance with the views generally held. The technics employed consisted in the use of formalin-hardened sections, stained for from one to twenty-four hours in methylene blue, dehydrated in alcohol, cleared in oil of cajeput, and mounted in Canada balsam.

In such sections the anastomoses between nerve cells is by no means uncommon. For the most part this consists of a common dendrite which connects the protoplasm of one cell with that of another. Usually this process is short, but often it may attain to a comparatively great length. The common dendrite is in every way similar to that ordinarily observed. It arises by a broad base from one cell, and its connection with the other is marked by a similar base. The Nissl bodies are clearly visible in the dendrite. Thus far, anastomoses have been observed only between cells of the same group, and never between cells of different groups. Golgi's method has also been employed and has several times shown anastomoses between three cells, while in one case five cells were apparently connected together. Anastomoses have also been found by Golgi's method in the cerebral cortex and basal ganglia of the white rat.

Sala, working with Golgi's method, has put forth the claim that the dendrites imbed themselves in the blood vessels. His position has been severely criticised by Lenhossèk. That the dendrites do actually imbed themselves in the walls of the capillaries is to me an established fact. The tip of the cell process before it connects with the wall of the capillary widens out into a wedge-shaped end. This condition leads me to believe that the dendrites have besides the generally conceded nervous function, also nutritive function.

April 6, 1899.

DIFFUSE SARCOMA OF THE CEREBRAL AND SPINAL PIA MATER.

GEORGE H. WEAVER.

Tumors of the soft membranes of the brain and spinal cord, especially those of a diffuse character, are comparatively rare, and a careful study of each individual example is of distinct value. The following case was kindly offered me for study by Prof. Ludvig Hektoen, to whom I am indebted for much assistance in the preparation of my report.

Primary tumor of cerebrum, secondary diffuse sarcoma of the cerebral and spinal pia mater.—W. C., male, aged 11 years, entered the Presbyterian Hospital December 31, 1896, in the service of Dr. A. C. Cotton. Clinical diagnosis, tubercular meningitis.

Family history negative. No tubercular or specific history obtainable. Present illness began September, 1896, with convulsions, in which the whole body was rigid and the eyes fixed. Before the convulsions the patient was dizzy and vomited; after them he would sleep for a time, and upon waking would be delirious. At times he was confined to bed.

Examination on admission: Confined to bed, poorly nourished, skin warm and moist, countenance staring and flushed at times, pulse regular and rapid, Cheyne-Stokes respiration, bowels constipated, pain in head and neck; only partly conscious, moves but little, but there is no paralysis; eyes bulging, pupils widely dilated, sight much impaired, the right eye insensible to light, the left to sensation; nystagmus marked, double optic neuritis; temperature 98.8 F., pulse 100. Hyperesthesia over entire body. Pain on percussion over the cranium. *Taches cerebrales.* From this period until death there were recurring paroxysms, sometimes several in a day, and again only at intervals of several days. There were, later, delirium and involuntary evacuations. Death took place April 13, 1897.

AUTOPSY BY DR. HEKTOEN.

Body small and extremely emaciated; head large; thyroid gland large. Larynx and trachea normal. Pleuræ smooth and empty. Over the anterior surface of the right lower lobe is a circumscribed area in which the pleura contains numerous grayish-yellow, pinhead and larger, disc-like nodules. The peribronchial lymphatic glands contain tubercular areas. Lungs normal save for circumscribed areas of grayish-red consolida-

tion in the lower lobes. Heart small; endocardium and myocardium normal; pericardium smooth. Aorta normal. Spleen, kidneys, pancreas, liver, stomach, intestine and adrenals normal. Mucous membrane of urinary bladder red, rough and covered with shreddy material.

Upon opening the cranial cavity a large amount of very slightly turbid fluid runs out. Dura mater normal. The pia mater upon the optic commissure, the medulla and the upper part of the spinal cord is the seat of a reddish, indistinctly nodular thickening. Around the apex of the left frontal lobe is a similar area. The entire posterior surface of the spinal cord is the seat of marked thickening, so that the pia is reddish and somewhat lobulated, and the volume of the cord appears to be greater than normal. It fills the dura, and when the latter is cut masses are forced out through the opening. The ventricles of the brain are greatly dilated, containing a clear fluid.

Anatomical Diagnosis.—Sarcoma of pia mater, of brain and spinal cord. Hydrocephalus. Broncho-pneumonia. Acute cystitis. Chronic tuberculosis of the peribronchial lymph glands and pleura.

Description of the Brain.—There are irregular areas of a gelatinous, opaque, whitish-gray substance in the pia mater, scattered over the anterior surface of the medulla and the pons and spreading out over the lower surface of the lobes of the cerebellum. The largest area upon the cerebellum is on the right lateral hemisphere, being 4.5 cm. from before backward and 2 cm. wide at the thickest part. This lies parallel to the fissure between the lateral and median lobes, extending outward from the fissure. This area is not elevated above the surface but appears to involve the underlying substance. From this area a thinner growth extends continuously over the lower surface of the median lobe, becoming less dense as it approaches the left lobe. Upon the left lobe, lying in a position symmetrical to that on the right, is an area of growth 1.5 cm. antero-posteriorly and 0.75 cm. transversely. This is slightly elevated above the surface and somewhat firmer than the corresponding area on the opposite side. Scattered over the under surface of both lateral cerebellar lobes and along the front of the medulla and pons are areas of growth varying in size from those which are very minute to those 0.5 cm. in diameter. The largest of these are elevated above the surface and are firmer than the larger areas upon the cerebellum. They appear to bear no relation to the vessels in their distribution. On the upper surface of the optic commissure and optic nerves at their origin are globular masses of growth 0.5 cm. in diameter, which are partly continuous, thus forming an irregular, uninterrupted mass along the optic commissure and nerves. The apex of the left cerebral hemisphere is soft and somewhat

collapsed. The surface for about 3.5 cm. from the apex, on all sides except below, presents the same sort of growth as that found on the cerebellum. It is, however, of a more pinkish-gray color. The tissue underlying this surface growth is very soft. A few small discrete masses of growth are seen at short distances from the larger area over the surface of the left cerebral hemisphere.

The brain was hardened in Müller's fluid containing 5 per cent. of formalin. On cutting the left cerebral hemisphere into vertical sections, each 2 cm. thick, it is found that the centrum ovale of the left apex is replaced by a tumor extending antero-posteriorly 5 cm.; its diameter at a depth of 2 cm. is 5 cm. and at a depth of 4 cm. is 4 cm. The growth is extremely soft, and of a pinkish-gray color. In the sections the tumor mass tends to fall away from the surrounding tissue. The lateral ventricle is empty, very much dilated, its wall smooth, and the choroid plexus unaltered. Corresponding sections of the right hemisphere show the lateral ventricle to be similar to the left. This hemisphere is otherwise normal.

The fourth ventricle is filled to distension with a reddish and in parts grayish tumor mass. This is very soft, contains much blood and is continuous with the walls of the ventricle. It measures antero-posteriorly 4.5 cm., transversely 3.5 cm., and vertically 2.5 cm.

The Spinal Cord.—The cord, which was hardened in 5 per cent. formalin, appears very much enlarged in the dorsal and lumbar regions. In the lower dorsal region it measures 1.75 cm. antero-posteriorly and 2.5 cm. transversely. The growth externally is slightly nodular and uneven, opaque and whitish-gray. In the upper dorsal region the blood-vessels are large and prominent. The growth extends over and between the nerves of the cauda equina. On section the cord itself is found to be of about normal size, the apparent enlargement being due to a growth of new tissue about it. The tumor growth is most abundant posteriorly, and is thickest in the lower dorsal and lumbar region where it is 0.75 cm. in thickness; it becomes much thinner in the cervical and upper dorsal regions. The growth in front of the cord also extends throughout the entire length, being more largely developed in the lower dorsal and lumbar regions. It is nowhere more than 1 or 2 mm. thick. Laterally the growth is more abundant in the lower portion of the cord, where it is from 2 to 3 mm. thick and completely surrounds the posterior roots and to a less extent the anterior roots of the spinal nerves. The posterior roots appear very large from the tumor deposit. In the upper part of the cord the lateral growth exists as a very delicate, thin layer.

MICROSCOPIC EXAMINATION.

Spinal Cord.—Weigert's stain. The cord is usually normal

except in some places along the posterior border, where it is invaded for a short distance by the tumor.

Hematoxylin and eosin. The tumor is usually sharply limited at the border of the cord by a fibrous structure consisting of the altered pia mater. There is a growth of tumor tissue along the normal trabeculæ which passes from the pia mater into the cord. Posteriorly the cord is directly invaded by the tumor for a short distance. The tumor is everywhere of the same structure, consisting of closely-packed, small, round cells, with deeply-staining nuclei. The intercellular structure is usually but little developed, and in most places appears as a homogenous material, staining faintly with eosin. Where the cells are not so closely packed it is finely fibrillated. In some places the connective tissue framework is more largely developed, appearing as quite heavy bands, but with little tendency to any regularity of arrangement. The blood-vessels are large and numerous with well-developed walls. In the cervical and upper dorsal region the tumor is less than in the lower parts, but exists upon all sides. It is here thinnest at the sides and most marked posteriorly. The nerve-roots are here more or less surrounded by the growth, which has not penetrated the nerves themselves. In the lower dorsal and lumbar regions the growth is also least laterally and most developed posteriorly. The posterior nerve-roots, and to a less degree the anterior roots, exhibit an infiltration of the epineurium and perineurium, but the endoneurium has not been invaded by the tumor. Some of the larger vessels and bands of fibrous tissue have undergone hyaline degeneration. In the cauda equina the growth surrounds the nerves, but only in a few places was the endoneurium penetrated by tumor cells.

Brain.—The tumor in the apex of the frontal lobe consists of small round cells with deeply-staining nuclei, like those in the spinal growth. The arrangement of the vessels and the trabeculæ of the fibrous framework produces a somewhat alveolar appearance in places. The growth in the cerebral pia mater is similar to that in the spinal.

Sections were made of the tumor growth in the fourth ventricle, including the adjacent cerebellar tissue with its covering of pia mater, which appeared very slightly thickened. There is everywhere a thin layer of new growth following the pia mater over the convolutions of the cerebellum. The cells penetrate to a very slight extent the brain substance. The blood-vessels are very numerous, many being of large size. There are large and small areas of hemorrhage into the tumor, some being quite recent with well-preserved blood corpuscles; others old, with remnants of blood-cells, fibrin and blood pigment.

Lungs.—In the lungs, on and near the pleura, are small areas of tubercular infiltration, containing foci of caseation, giant

cells and tubercle bacilli. In the lungs are some areas of cell accumulation which resemble those in the tumor of the brain and cord. In these no caseation or giant cells are seen. From the histology of these areas it is impossible to decide whether they are metastatic tumors or not.

I have collected from the literature ten reports of diffuse meningeal sarcoma, of which the following are abstracts:

1. (Coupland and Pasteur.[1]) Female, aged 22 years. Course of illness about four months. Began with headache and morning sickness; later there were pains in the right shoulder and arm. A month before death pain along the spine; two days before death constant occipital pain radiating to the right shoulder and arm, double optic neuritis, paralysis of both external recti, tenderness of scalp, hyperesthesia along the spine, weakening but not paralysis of the legs, and absence of knee-jerk; sphincters acted normally; no convulsions.

Autopsy.—Soft, jelly-like masses of new growth scattered over the meninges beneath the dura in the posterior fossa, about the body of the sphenoid and backward almost continuously to the foramen magnum. Medulla and pons uniformly invested with similar growth in which both sixth nerves were completely embedded. Spinal cord uniformly ensheathed in a semi-translucent, softish growth of a grayish-white color, the tumor being most developed on the posterior and lateral aspects of cord. Nerves of cauda equina surrounded by thin sheaths of new growth, which at intervals expanded into small tumors. The cord itself normal in shape and appearance throughout. The new growth was a small round-celled sarcoma, which followed the trabecular ingrowths of the pia into the cord. Brain normal.

2. (Coupland and Pasteur.[1]) Female, aged 4½ years. Duration of illness about three months. Following a fall the child became irritable, developed a squint, and at the end of a month was unable to walk. Pain in upper part of back and head was followed by sudden blindness six weeks from the onset. Two months from the beginning was conscious and intelligent; pupils dilated and insensitive, blindness, pain in back and head. Optic discs gray and indistinct. General muscular weakness without atrophy, normal tactile sense, *taches cerebrales*. No convulsions.

Autopsy.—A layer of grayish material covered the under surface of the cerebellum over the middle and part of the lateral lobes, varying in thickness and extending for about half an inch into the nervous tissue. Middle lobe almost entirely replaced by a soft, gray, vascular growth. Pia-arachnoid over medulla and pons normal. Thin layer of new growth on left side of optic chiasm and nerve, with similar patch, about the

size of a pea, on under surface of left lower temporal convolution. Lateral ventricles greatly distended. Basal ganglia normal. Spinal cord appeared enlarged at upper part with small scattered hemorrhages in the gray matter. Posterior aspect of the cord covered throughout by new growth ¼ to 1/5 inch thick in lumbar region. The tumor was a small round-celled sarcoma.

3. (Olliver.[3]) Male, aged 11 years. Duration of disease about six months. There were paroxysmal headaches, retraction of head, convulsions, and later vomiting. Two days before death blindness with dilated pupils and pains in the limbs. The day before death acute pains throughout the body, but conscious. Convulsions, constipation and nausea; no vomiting.

Autopsy.—There was a uniform pinkish formation extending over the posterior surface of the cord, averaging one line in thickness, thinner toward lateral aspects of the cord and blended with arachnoid. It was fairly firm, like unsoftened cerebral tissue, and traversed by small blood-vessels. There was a tumor in the cerebellum.

4. (Hadden.[4]) Although described as chronic cerebro-spinal meningitis, this case was evidently one of diffuse meningeal sarcoma. Male, aged 13 years. Duration 14 to 17 months. An injury to the head 17 months before death was followed by pain in the head and vomiting. Fourteen months before death sickness in the morning, pain in the head, fainting and attacks of dizziness. Two or three months before death weakness of legs, loss of control over bladder, convulsions, followed by stupor, occurring as frequently as 4 or 5 times a day and ceasing a few weeks before the fatal ending. The patient was drowsy and nearly blind, the pupils being equal, dilated and sluggish. Temperature usually normal or subnormal, being only twice above 100 F.

Autopsy.—Under surface of cerebellum almost entirely coated with an opaque white material varying in thickness from 1 to 4 mm. Upper surface of cerebellum and adjacent parts of the cerebrum similarly but less extensively affected. Tips of temporosphenoidal lobes showed the same condition in a minor degree. Much thickening and white opacity about optic tracts and chiasm. Lateral ventricles distended with clear fluid. No tumor in the brain. Beneath arachnoid on posterior surface of lower dorsal and lumbar cord a thick, white layer similar to that upon cerebellum, which presented numerous bleb-like elevations. Cervical and upper dorsal cord free.

The white thickening over cerebellum and cord consisted microscopically of round and spindle-shaped cells with a considerable amount of new connective tissue in interlacing bundles. The vessels were large. No tubercles.

5. (E.L. Fox.[5]) Male, aged 29 years. Duration of disease not given (patient came to hospital after being sick for three

months, and probably did not live long afterward): began with shooting pains in arms. Gradual flexion of fingers developed. Difficulty in urinating and priapism. On admission anesthesia of legs, thighs, abdomen and chest to third rib, and paralysis of lower extremities.

Autopsy.—The cord seemed generally larger than normal with a marked swelling posteriorly at its upper portion midway between cervical bulb and second cervical vertebra. On section this was found to be a tumor, 1½ inches long and ¾ of an inch broad, with well-defined margins of a purplish color and tolerably firm. Cord smaller than normal, the great apparent increase in size being due to a layer of yellowish-gray substance fully ¼ of an inch thick; enveloping cord on all sides. This growth extended from highest portion of cord to cauda equina. In pia mater covering pons and medulla much thickening and rounded masses of exudate extending along the vessels as far as fissure of Sylvius.

Microscopically the tumor was a spindle-celled sarcoma.

6. (G. H. Bennett.[5]) Male, aged 48 years. Duration about 11½ months. Began with weakness in legs. No headache or other cerebral symptoms except dizziness. Vision good. Dull aching in back and lower limbs. For six weeks before death patient could not stand; suffered from constant severe pains in legs and from attacks of uncontrollable vomiting.

Autopsy.—Areas of softening in cerebrum and cerebellum. Pia mater of cord thickened, especially its posterior aspect, most marked below and gradually diminishing upward. Posteriorly, membrane studded throughout with round and oval, isolated and confluent, white nodules, varying in size from mustard seed to pea. These growths surrounded posterior roots. None visible to naked eye in front or laterally. The growth was a round-celled sarcoma.

7. (Westphal.[7]) Female, aged 15 years. Duration a little over a month. At first headache, dizziness and pain in back, and two weeks later convulsions. Mind dull, pupils irregular, slight paresis, pain over spine on percussion, no choked disk. Before death severe headache, dizziness, vomiting, paralysis of ocular muscles and absence of knee-jerk. No fever. Death took place in a convulsion.

Autopsy.—Grayish-white and in parts more reddish thickening of pia-arachnoid, extending from optic chiasm backward over pons and medulla and outward somewhat over temporal lobes. Cranial nerves more or less imbedded in tumor thickening. Lateral ventricles contained blood-tinged fluid. In and near left optic thalamus three firm, smooth tumors of a red and grayish-white color, one being connected with tela choroidea. Pia-arachnoid of cord especially posteriorly, presented grayish-red tumor growths, slight above, but increasing downward, becoming in dorsal region a promi-

nent covering. Cord itself normal. Metastatic nodules in lung.

The tumor was a richly nuclear, round-celled sarcoma, with numerous vessels scattered between the cells. The cord was not invaded. The spinal nerve-roots were imbedded in but not invaded by the growth. The tumor had implicated the cranial nerves.

8. (Virchow.[8]) Male, aged 30, copper-worker; attacks of colic, paresis and toward the last almost total blindness.

Autopsy.—On surface of hemisphere single yellowish-brown pigment spots. At base of brain a more diffuse, confluent deposit in the soft membranes of a melanotic material, extending laterally and thickest between chiasm and pons. At apex of middle lobe and on sides and middle of cerebellum growths as much as 3 lines in thickness. Diffuse growth along various cranial nerves, optic and olfactory being imbedded in it. The growth extended into the nerves and completely infiltrated the Gasserian ganglion, but did not extend beyond the foramina. Eyes normal. On posterior surface of cord in upper part isolated, flat, almost black tumors; below in dorsal and lumbar regions these became continuous, the cord being covered by a layer of growth three lines thick. In cervical portion, posteriorly and laterally and in front throughout, only blackish-brown pigmentation was apparent. Nerves of cauda equina and most of other spinal nerves covered by growth forming in places nodules. The tumor was a round and spindle-celled melanotic sarcoma. In a few places pigment was absent.

9. (G. Lentz.[9]) Male, aged 23 years. Duration about 12 months. Began with pain in back, later in arms and legs; weakness of muscles, first in legs, later in arms and trunk. At the end of 6 months pain and tenderness on percussion over spine and exaggerated patellar reflexes. Optic neuritis with normal pupillary reaction. One month before death patient was bed-ridden, mind dull, pupils irregular and sluggish, bilateral, choked disk, marked paresis and atrophy of muscles. Patellar reflex present on right side only. Sensibility reduced in legs, arms and parts of back. Later vomiting and cystitis.

Autopsy.—There was a tumor involving corpus callosum and laterally invading the hemisphere. Lateral ventricles distended with fluid. A cavity in upper part of cord. Whole posterior extent of cord covered by a pale gray mass about 1 mm. thick. In dorsal region growth extended to the sides of cord. From lumbar region downward whole cord encased in a gray, homogeneous, jelly-like mass 0.5 cm. thick. Cord was of normal appearance only in the lower portion.

The mass of the tumor consisted of closely-packed, short, oval or roundish cells, separated by scanty interstitial tissue, in places distinctly fibrillated. There were abundant vessels with well-developed walls, some having undergone hyaline

changes. The pia was usually sharply differentiated from the cord, and in places the tumor penetrated along the pial septa. Here and there the connective tissue was arranged so as to form a meshwork in the spaces of which the cells were accumulated. Large cells of endothelial type were found singly and at times in groups. Limited portions of cord were directly invaded by the tumor. The cerebral tumor was of similar structure and hemorrhagic.

10. (R. Schulz.[10]) Female, aged 16 years. Duration about 3 months. Severe pain in back, numbness and formication in hands and arms, with increasing weakness in arms, which were paralyzed shortly before death. Patient conscious up to the last. Pain in head, nutrition good, inability to stand, hands red and swollen, tenderness on pressure over main nerves of trunk and upper limbs. No affection of cerebral nerves. Marked tenderness over whole spine, retention of urine, constipation; anesthesia of both upper limbs and absence of the patellar reflex on right side. Clinical diagnosis was acute meningo-myelitis.

Autopsy.—Cranium and its contents normal. On opening spinal dura cord bulged, presenting a sausage-like appearance. Sub-arachnoid space occupied throughout by grayish-red mass of growth, covered by delicate arachnoid, nodular and lobulated, partly firm, in places soft and studded with hemorrhages. In lumbar and lower dorsal regions growth completely ensheathed cord, while in the upper part it covered only posterior surface. At one point it penetrated the cord.

Microscopically growth was made up of large endothelial cells traversed by numerous capillaries which gave it an alveolar character. It is described as an alveolar sarcoma.

Of the 11 cases, including the one here reported, in which there was a diffuse sarcomatous growth in the pia mater of the cord and base of the brain, in 6 there was no tumor of the nervous structures which could be considered primary (Coupland and Pasteur, Schulz, Hadden, Fox, Virchow). In the other five there was tumor growth in either the cerebrum, cerebellum, pons or basal ganglia. In all of these cases the macroscopic characteristics were very similar, as was also the distribution. In the cranial pia mater the growth was most abundant about the optic commissure and over the cerebellum, and spread here and there to the surface of the lower portions of the cerebrum. It usually extended more or less along the cranial nerves. The spinal growth

was most extensive along the posterior surface of the lower part of the cord. The posterior growth was comparatively slight in the upper part, as was also that in front and to the sides of the cord throughout the entire length. The tumor tissue was yellowish or grayish-white, with more or less of a pink or red color in some cases. The consistence varied, but was usually rather soft.

The microscopic characters of the tumors from the various cases have differed somewhat. Virchow's case is the only one of a melanotic growth. Schulz reports his case as one of alveolar sarcoma. In Hadden's case the tumor is said to consist of round and spindle cells, and Fox's was one of spindle-cell growth. In the two cases of Coupland and Pasteur, in those of Bennett, Lentz and Westphal, and in my case, the tumor was a small, round-celled sarcoma. In some of the cases the blood-vessels are spoken of as being large and abundant. There was usually little or no tendency for the growth to invade contiguous structures. The cord was rarely involved, and then only to a slight degree; the brain was more apt to suffer. The growth, however, showed a special tendency to infiltrate the pia mater even to its finest processes and prolongations. The cranial nerves were occasionally invaded by the tumor cells, but the spinal nerve-roots, even when imbedded in a mass of tumor tissue, were only occasionally directly attacked.

The variety of diagnoses made *intra vitam* in the reported cases indicates the divergent character of the clinical manifestation. This is largely due to the wide diffusion of the lesions and the association in many of the cases of symptoms produced by one or more tumor nodules in the brain. In my case the large growths in the cerebrum and fourth ventricle had not given rise to symptoms, and it was thought by the clinicians who had studied the case that localized tumor could be excluded from the diagnosis.

The ages of the patients varied from 4½ to 48 years. Of those in which the age is recorded, 6 were under 20 years and only one above 30 years. The course was usually tolerably rapid, the fatal termination being reached within a few months. Pain in the head and back was an early symptom. There were often pain and hyperesthesia in the extremities, followed by muscular weakness, and later paralysis. Constipation was sometimes followed by incontinence of feces and urine. Paralysis of the ocular muscles, partial or complete loss of sight and optic neuritis were noted. The temperature was not usually above the normal. In the early stages consciousness was often unimpaired, but later was sometimes much disturbed.

October 11, 1897.

BIBLIOGRAPHY.

1. Trans. Path. Soc., London, 1887, xxxviii, 26.
2. Ibid.
3. Traité des maladies de la moelle épinière, t. ii, p. 490, obs. cxxviii, Paris, 1837.
4. Trans. Path. Soc., London, 1885, xxxvi, 13.
5. Bristol Medico-Chirurg. Journal, 1883, 1, 104.
6. Trans. Clin. Soc., London, 1885, xviii, 168.
7. Archiv. f. Psychiatrie, 1894, xxvi, 770.
8. Virchow's Beiträge, 1859, xvi, 180.
9. Ziegler's Beiträge, 1896, xix, 663.
10. Arch. f. Psychiatrie, 1885, xvi, 592. (Abs. in Trans. Path. Soc., London, 1887, xxxviii, 32.)

A CASE OF GLIOMA CEREBRI.

HUGH T. PATRICK AND MAXIMILIAN HERZOG.

Clinical Report by Dr. Patrick.

M. Z., a girl of 16 years, saleswoman, was first seen April 8, 1895. The previous July, that is, nine months before, she had two general convulsions which are said to have lasted about an hour. After this she had an attack similar to the others. They were all said to begin with a choking sensation that seemed to rise from the abdomen or epigastric region. After this third fit she again remained comparatively well

till near Christmas, when right-sided headache appeared and about the same time she began to suffer from occasional attacks of a peculiar jerking that started in the left hand and arm and spread to the face. They were not attended with loss of consciousness or even mental confusion, as the patient would call the attention of her companions to them and try to control the spasm by grasping the affected hand with the other.

The jerking lasted only a few minutes and always left the arm and hand rather weak for a short time. On account of these attacks which gradually became more frequent, and the following weakness, as well as on account of the increasing severity of the headache, she was unable to work steadily after January, but had held her place until a short time before I saw her.

She had been seen by several physicians, but the convulsions, as well as the local spasms, were so irregular and peculiar and the persistent headache so unaccountable that she was thought to be suffering from hysteria—that ample shroud which covers so many clinical pictures.

I found the patient in bed complaining of excruciating pain over the right side of the head. There seemed to be some mental hebetude but whether this was due to the disease or the pain or to the anodynes that had been given for the headache, it was hard to tell. She was quite rational, however, answered all questions clearly and executed all commands to the extent of her physical ability. There was weakness, inco-ordination and diminished tactile and pain sense on the left side and diplopia that seemed to be due to paresis of the right external rectus. Hearing was normal, but vision was impaired and the ophthalmoscope revealed intense double optic neuritis.

A diagnosis was made of tumor near the arm center, probably deep (that is not cortical) and probably not specific, as there was nothing in the examination or history to indicate syphilis.

Operation was advised and it was done a couple of days later by Dr. N. Senn. A large opening was made over the arm center, the dura was normal in appearance, tense, bulging and distinctly pulsating. The result of palpation was negative and a small nick made in the dura allowed a few drops of clear serum to escape. The wound was closed and rapidly healed.

After the operation there was no headache, diplopia, hebetude, convulsions or jerking and the vision improved. The patient remained well, comfortable and happy, except for some weakness of the left side, for three months. At the end of this period, however, the headache suddenly returned and I saw her again for the first time since the operation. At the site of the operation there was considerable bulging that pulsated distinctly. Left hemiparesis with some inco-ordination existed as did also double-choked disc, although both were less marked

than at the time of operation. Potassium iodid and phenacetin afforded relief from the pain for a short time, but it returned and the parents arranged for a second operation.

When the surgeon learned that the patient had never received full antisyphilitic treatment he advised a trial of that first, and from this treatment the headache abated for about another three months, although the paresis and ataxia of the left side rather increased. During this time she passed into other hands and I lost sight of her. Her last medical attendant was Dr. Ochsner, who operated several times for the relief of pressure and to whose kindness I am indebted for the specimen. The tumor proved to be a subcortical neoplasm, about the size of a child's fist, situated just behind the arm center and covered by an extremely thin layer of cortex which at one place had almost been broken through.

Histological Report by Dr. Herzog.

Small pieces from several regions of the tumor which had been hardened in Mueller's fluid were dehydrated in alcohol, embedded in celloidin and stained with hematoxylon-eosin, borax-, pioro- and uranium-carmine. Neither Mallory's nor Weigert's neuroglia stains could be used, since the tumor had been hardened in Mueller's fluid, and had only been obtained considerable time post-mortem.

The microscopic examination of the tumor shows it to be a pure glioma, a neoplasm of the neuroglia. The examination was made on sections and also on teased tissue. The latter was obtained by dissolving the celloidin with oil of cloves out of sections which were then teased.

The neuroglia, in a functional, but by no means in a histogenetic sense of the word, the connective tissue of the central nervous system, has for several years been extensively studied and has lately become the object of a very lively controversy. It is now unanimously conceded that the neuroglia is of ectodermal and not of mesodermal origin, and we therefore have to classify neoplasms of it among the epiblastic and not as has formerly been done among the mesoblastic new growths.

The contested point concerning the neuroglia is whether its fibers are cell processes or are fibers which have no connection whatever with cells. Kœlliker, Ramon y Cajal, Golgi, Lenhossèk and others hold the former view, while the most prominent exponent of the latter, long ago expressed by Ranvier, is Weigert. This investigator has devised a specific new neuroglia stain which stains the neurogliar fibers but does not stain the cell protoplasm. Weigert, on the strength of this tinctorial test, with perfect propriety, holds that the fibers are chemically well differentiated from the cell protoplasm and from this he concludes that they can not be processes of the former. In Kœlliker, "Gewebelehre," vol ii, Leipzig, 1896, p. 791, there may be found an extensive, very interesting discussion of this question which naturally is of interest, not only with reference to the normal, but also with reference to the pathologic anatomy of the neuroglia.

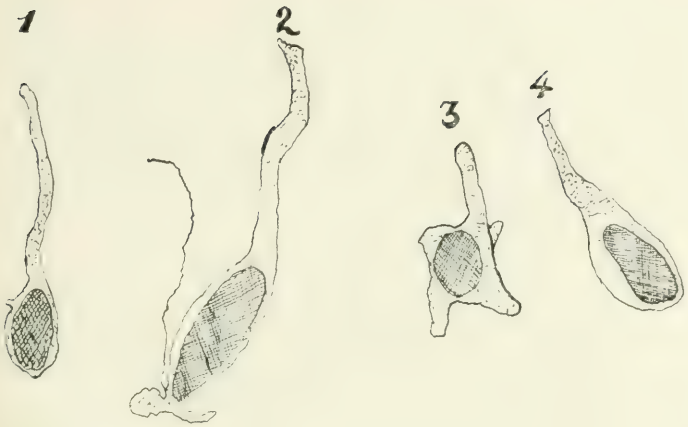
Strœbe, who has published one of the most extensive monographs upon gliomata, belongs to those who maintain that the fibers are cell processes. He believes that gliomata as a rule, at least, if not always, originate from embryonic inclusions derived from the central canal and lined with ependymal epithelium. In one of his cases Strœbe found cavities lined with such cells. While this author looks upon gliomata, even if—as is usually the case—a certain number of ganglionic cells and axis cylinders are found, as a new growth of the glia only, Klebs calls the tumors under discussion neuro-gliomata, because he thinks that they are neoplasms of the neuroglia as well as of the nervous elements proper (ganglion cells, axis-cylinders). Klebs' view has been supported by some subsequent observers, namely, Meyer and Beyer, and Volkmann. Cases of gliomata have recently been studied by Taylor, and by Thomas and Hamilton, both their contributions having been published in the last volume of the *Journal of Experim. Medic.* Tay-

lor endorses Weigert's view concerning the neuroglia fibers.

That the gliomata of the retina are also neoplasms of the neuroglia—which had been doubted by some—has some time ago been shown by Greeff, who utilized the material of Schweigger's eye-clinic, and who published his report in the *Deutsche Medizinische Wochenschrift,* (1896, p. 327).

The tumor, the clinical history of which has been given by Dr. Patrick, consists of densely packed neuroglia cells, which show a great deal of polymorphism. The vesicular nuclei vary from a spherical to an elongated oval shape. The amount of protoplasm surrounding the nuclei likewise varies very much between the limits of a mere very narrow covering to quite an extensive cell body. The nucleus shows a fine deeply staining reticular network, the cell protoplasm is finely granular. Many of the neoplastic neuroglia cells are quite atypical in shape. They are fusiform and bipolar with one or two, or more, well-marked protoplasmic processes, *which do undoubtedly arise out of the cell body.* Other cells apparently give a very good picture of the two different types called "Kurzstrahler" and "Langstrahler" by Kœlliker. The cells are embedded in a dense felt of fibers, but the former are almost everywhere very numerous, so that we do not have to deal with a gliomata which might properly be called a fibroglioma, such as has been described by Strœbe, and recently also by Taylor, who reports, "that the essential and striking feature of the tumor is the presence of fibers whose number is out of all proportion to that of the cells."

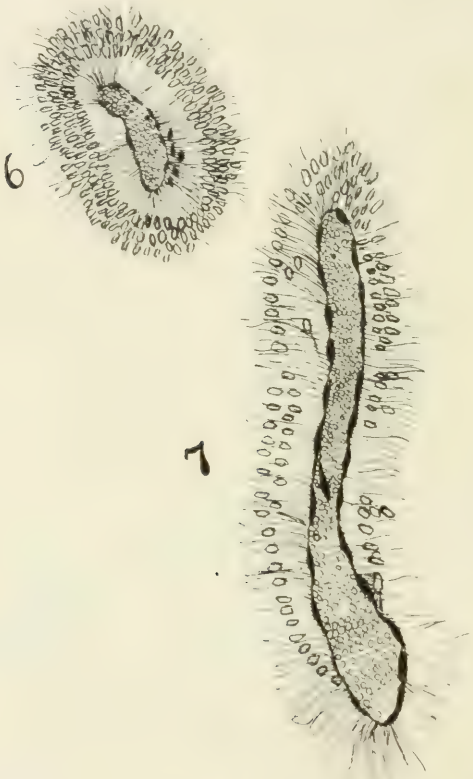
In our case the cells are comparatively scanty in a few places only; as a rule they are densely packed side by side. The new growth is very rich in blood-vessels. It appears that those blood-vessels are surrounded by a thick hyaline mantle or sheath. In teased sections and



No. 1, 2, 3 and 4.—Camera drawing, Reichert's hom. oil imm. 1 12 inch, eye-piece No. 4. Cells with large processes, which clearly show how the latter arise out of the cell protoplasm. No. 2 shows a fine fiber which is probably not connected with the cell protoplasm, but only adherent to it.

No. 5.—Magnification as above. Fine neuroglia fibers intermingled with cells; the latter do not show any processes and the fine fibers are not connected with the cell protoplasm, they either run above or below the cells or have no relation at all with the latter.

under higher magnifying power it becomes evident that what appears to be a hyaline sheath is made up of numberless densely packed fibers of varying caliber, being all attached on one side to the blood-vessel wall,



No. 6 and No. 7.—Reichert's obj. No. 3, eye-piece No. 4. Bloodvessel[s] showing how the neuroglia fibers are attached to the vessel-wall, so that there is an apparently homogeneous hyaline sheath formed around the vessel. The fibers can be seen best in No. 7, which is drawn from a blood-vessel which had been torn loose from the surrounding tissue.

while some of the fibers are connected on the other side with neuroglia cells. A proliferation of the elements forming the blood-vessel wall proper is not found. The tumor, therefore, is a pure glioma and does not show any of the features of a so-called glio-sarcoma. Axis-

cylinders and ganglion cells were not found; there was, however, no particular effort made to find them. If present at all, they are not to be found in large numbers.

With reference to the neuroglia fibers, the tumor demonstrates beyond a doubt that the large, thick, heavy fibers are processes of the cell protoplasm. It is, however, impossible to make the same claim with reference to the long, slender, thin fibers. They seem to be unconnected with any cells, and where they do appear to be in relation with a cell, they, in fact, stretch either above or below this cell. I am of the opinion that the neurogliar fibers are derived from the glia cells by a process very similar to that which leads to the formation of a cornified scale from an epidermal cell.

That similar changes of maturity and senility may go on in the cells of the epidermis and those of the neuroglia, unreasonable as it may appear on first sight, becomes more plausible, if we consider the common histogenic origin of these cells so very much different in their character in later life.

January 10, 1898.

REPORT OF THREE CASES OF BRAIN TUMOR WITH SPECIAL REFERENCE TO THE PATHOLOGY OF NEUROGLIOMA AND THE PSYCHICAL CHANGES CAUSED BY BRAIN TUMORS.

A. F. LEMKE.

1. Psammo-Sarcoma.
2. Tubercle.
3. Neuroglioma ganglionare.

CASE 1.—M. A., aged 45, Hungarian, coal-miner, was admitted to Illinois Eastern Hospital for Insane on January 5, 1897, with a rather indefinite history of mental impairment

that is said to have followed an attack of typhoid fever, although an injury to the head (a fall) and masturbation were assigned by his relatives as etiological factors. After his recovery from typhoid fever it was noted that he was becoming careless and dull with an occasional outburst of violence. His habits became very filthy; he seemed to have lost all interest in his surroundings and slept a great deal; he had not complained of headaches, nausea or dimness of vision; at least these had not been noted by the physicians in charge previous to his admission here. Great disinclination to psychical and physical exertion and loss of memory developed early in the history of the case. No delusions nor hallucinations. There is little of interest in the personal or family history of the patient previous to the attack. He used alcohol and tobacco to excess. For the clinical history of the patient after his admission here I am indebted to Dr. B. C. Bowell.

The patient is a well-developed man, 45 years of age. His attitude is careless and expression dull. The pupils are somewhat dilated but react normally to light and accommodation. No motor disorders of the eye muscles. Vision is apparently normal—the great mental dullness does not admit of a careful examination of the acuity and range of vision. Ophthalmoscopic examination could not be made.

Circulatory and respiratory organs are normal; pulse 72, regular and strong.

Digestive organs: Mucous membrane of mouth is pale; marked fetor ex ore; teeth are crowded and irregular. Involuntary defecation. No vomiting since admitted.

Sensory Symptoms: Patient complains of vertigo. No pain or paresthesia. Cutaneous sensibility normal. Localization good.

Motor symptoms: There is no paralysis, although the lower extremities show considerable paresis. A slight ataxia of the cerebellar type and a rather coarse tremor of the hands. The knee jerk is much exaggerated; no ankle clonus. The other muscle jerks and the cutaneous reflexes are normal.

Genitalia are normal. There has been an incontinence of urine for several weeks.

Psychical examination: The most marked psychical change is what may be termed psychoparesis or mental asthenia. There is considerable depression. Psychical and psychomotor reaction is much retarded. Emotional control is retained. Memory and imagination are markedly impaired. The patient's attention can be sustained with great difficulty only and then but for a short time. The working over (Umarbeitung) of sense-impressions requires unusual effort, and even then is possible but to a limited degree. He is confused, dull and stupid. No delusion nor hallucinations can be elicited.

The mental and physical condition of patient continued with

no further changes until March 3, 1897. At 5:30 p.m. on that day he complained of nausea, and shortly after was found in bath-room in an epileptiform seizure. Ten minutes later he vomited profusely. Unconsciousness continued until 6:50, when a second seizure occurred. Profound coma until death supervened at 8 p.m.

In the absence of a more reliable and extensive history as to vomiting, vertigo, headache, dimness of vision and convulsions and the demonstration of choked disc, brain tumor was hardly suspected. The symptom-complex of psychoparesis and the development of convulsions before death were responsible for the diagnosis of dementia paralytica.

The necropsy was made fourteen hours after death and recorded as follows: The corpse is that of a well-nourished male, 167 cm. in length; estimated weight, 200 pounds. The entire face, neck, shoulders and dorsum show a marked degree of lividity. The post-mortem lividity is developed to a marked degree. Pupils are equal and con-siderably dilated. Panniculus adiposus in the abdominal walls measures 2½ cm. in thickness. The heart, lungs, spleen, liver, kidneys and intestinal tract are normal except that all the organs show much passive congestion.

The calvarium is of normal thickness; the markings on the inner surface are of the usual depth. The dura mater is very tense. Its inner surface is rather dry, very smooth and in close contact with the cerebral convulsions.

The leptomeninges are perfectly transparent and comparatively dry. The pial veins contain only small quantities of dark fluid blood. The surface of the brain is rather dry; the sulci are almost entirely obliterated. A decided sense of fluctuation is imparted to the palpating finger. The ventricles are enormously distended with clear, colorless fluid. The ependyma is normal. Attached to the choroid plexus of the left lateral ventricle is a tumor mass of oval shape measuring 4 cm. in length. The mass tapers from its larger posterior extremity, which measures 1½ cm., to the narrow apex, measuring only ½ cm. Externally the tumor is quite smooth and shows only large irregularities.

The cut surface is of a grayish color with a few scattered hemorrhagic points. In some areas it is infiltrated with calcareous material. The tumor mass is adherent posteriorly and below to the thalamus opticus, but this body does not appear to be infiltrated. The anterior extremity is adherent to the corpus callosum and the left half of this commissure is considerably thickened. Aside from the results of pressure nothing further was detected.

Post-mortem diagnosis: Hydrocephalus internus; tumor cerebri; pleuritis adhæsiva chronica levis. Small pieces excised from portions of the tumor in which little or no calcareous infiltration had occurred, fixed and hardened in formalin, corrosive sublimate and absolute alcohol. Pieces from the calcareous portion were decalcified in dilute nitrid acid and phloroglucin.

The sections made from the tissue that was decalcified are made up largely of mature connective tissue and blood-vessels. Here and there areas are found between connective tissue bundles in which there are spindle-shaped cells. The blood-vessel walls are considerably thickened and there is quite an accumulation of spindle cells around some of them. In many areas calcareous material is still present. Many of the smaller vessels are much thickened and contain deposits of calcareous material that is especially noticeable in the media. Other vessels are entirely occluded and infiltrated with the lime salts. Here and there an area of calcareous material is found which seems to have no direct relation to the blood vessels; but few of these areas show a concentric arrangement. The larger posterior extremity of the tumor contains much less calcareous material and mature fibrous tissue. Sections from the area are rich in round and spindle cells. The largest and most elongated spindle cells stretch across the section in bands and do not seem to have any connection with blood vessels. There are all gradations, from round to spindle cells. Few laminated calcareous bodies, separate and distinct from the blood vessels, are found in this area.

There is still some doubt as to what properly constitutes a psammoma. The genuine primary psammoma is found in the pineal gland, the choroid plexus and on the membranes, especially the dura at the base. The so-called brain-sand formation is a physiological process in the pineal gland and the choroid plexus, and an abnormal increase of this brain-sand, or acervulus, often

gives rise to tumors usually no larger than a pea or cherry. It is this variety of tumors, if they can be called such, to which the term psammoma, or acerouloma, properly belongs[1]. Oppenheim[2] and many others define them in a rather indefinite way as tumors, in which calcareous material is deposited, and in accordance with this view many cases have been reported as psammoma which in reality were sarcomata, fibroma, gliomata, etc., in which lime salts had been deposited. It certainly does not seem correct to designate a sarcoma or a glioma as psammoma for the sole reason that it happens to contain more or less deposit of this kind.

The tumor in our case must certainly be looked upon as a sarcoma and, inasmuch as it contains so much calcareous material, it is safe to speak of it as a psammosarcoma. If either term, singly, were chosen for this growth, it should certainly be sarcoma; for a considerable portion of the tumor mass as well as the entire area of the corpus callosum, which was infiltrated with neoplastic cells, is entirely free from the calcareous deposits. Among the largest of the psammomata that have been reported are those of Arnold—psammoma of the plexus choroideus of the third ventricle, the size of an apple; Petrina—a large psammoma of the dura at the base; Blanquinque—a psammoma the size of a pigeon's egg, of the pineal gland[2].

It is difficult to determine, in this case, the part played by the lesion of the corpus callosum in the production of the psychical symptoms noted here. Only one or two instances are recorded in which an ante-mortem diagnosis of tumor of the corpus callosum was made. Bristow[3] reviews the subject and believes that tumors in this area can be diagnosticated when the following positive and negative symptoms are present:

1. The gradual progression of symptoms noted in nearly all brain tumors.

2. The absence or very incomplete development of the

general symptoms, such as headache, vomiting, neuritis, optica, apoplectiform or epileptiform attacks.

3. Marked disturbances of intelligence, stupidity, sopor and nonaphasic speech disturbances.

4. Hemiparesis, often combined with a slight paresis of the opposite side.

5. Absence of symptoms on part of cranial nerves.

In our case the internal hydrocephalus is sufficient to account for all the symptoms present.

Case 2.—Mrs. I. J., age 47, was admitted to the Illinois Eastern Hospital, July 2, 1897. The condition of the patient at the time of admission was such as to make it impossible for the clinician to make a thorough neurological examination and the history prior to her admission could only be obtained from friends whose observations of the case were necessarily very imperfect.

The illness began about ten months after her last confinement—in June, 1892. The first symptom is said to have been numbness of the entire left side, which continued as the sole symptom for four months until, at the end of this time, a complete left hemiplegia made its appearance. The eyes deviated to the right side; left pupil was dilated. The paralysis gradually disappeared and at the end of ten months from its onset the patient was able to leave her bed. More or less paresis of the left side remained for twenty-eight months and left her in a practically normal condition for five months. Then a second attack of left hemiplegia made its appearance, this time very gradually. Headache, vertigo, dimness of vision and very frequent vomiting were experienced from the beginning of the second hemiplegia and continued to the end. One year ago (July, 1896) general convulsions occurred, recurring, with varying frequency, to the time of her death. During the last year vomiting has been the most prominent of the general symptoms. Nothing definite could be learned as to the nature of the mental aberration except that her speech was hesitating and incoherent. There was impairment of vision and hearing, and marked loss of memory; no hallucinations.

At the time of admission the mental condition of the patient was one of extreme confusion and depression. She was very anæmic and poorly nourished. The physical examination is recorded as follows: There is a moderate exophthalmus, more marked in the left eye; arcus senilis; pupils are equal, dilated and react only very feebly to light; accommodation normal; the visual field is approximately normal in outline, but vision is dim. No muscular incompetency in either eye. Hearing is much impaired on either side but more so on the left. Muscles

of left side of face are paretic. Fibrillary twitchings in muscles about the mouth and chin.

The chest is well developed; lungs negative. Area of heart dulness normal, pulse 48; some sclerosis of radials. The heart sounds are forceful and distinct; an occasional reduplication of second sound. Sphygmographic tracing shows distinct elasticity waves with only a bare suggestion of the dicrotic wave.

Examination of abdomen negative, except that the abdominal reflex could not be elicited.

There is universal muscular weakness but no distinct paralysis. Sensation is normal. Knee-jerk is absent; no ankle clonus.

The gynecological and urine examination are negative.

There is a marked ataxia when the eyes are closed and a tendency to fall toward the right.

No illusions nor hallucinations. After admission the patient grew worse quite rapidly. The pulse became very weak, but remained slow until, shortly before death, it reached 108. About three hours before death there was a typical pulsus alternans, the alternate small elevations being almost imperceptible and auscultation of the heart revealed the corresponding alternately forceful and weak contractions. Exitus lethalis at 2:30 p.m., July 18, 1897. Necropsy was made one hour after death.

The heart, liver, spleen and kidneys were normal. The left pleural cavity was entirely obliterated by readily separable adhesions. The lungs were somewhat emphysematous and the bronchi contained much very viscid turbid mucus.

The post-mortem findings in the head are recorded as follows: The calvarium is symmetrical, the sutures distinctly marked. The inner surface of the calvarium is quite rough. The frontal bones are relatively thicker than the others, measuring from 9 to 10 mm., whereas the occipital measures but 6 mm. The dura mater is tense, its internal surface rather dry. The surface of the brain is dry and the cerebral convolutions decidedly flattened. The cerebellum is somewhat atrophied. The basal vessels contain a few nodules of sclerosis. The left pedunculus cerebri is much larger than the right and is soft. The left optic tract is thinner and more ribbon-like than the right. The left temporo-sphenoidal lobe is relatively large and soft, except at its tip, where the consistence is increased. The pia mater is apparently not altered. The entire ventricular cavity contains a great excess of fluid; its ependyma is not altered except in the left descending horn, where it is very much softened and presents a roughened hæmorrhagic surface with many fissures, the latter the result of manipulation. Almost the entire left temporal lobe is soft. At its tip, involving principally the gyrus uncinatus, is a firm tumor mass made up of a grayish yellow, rather firm center, which is rather irregular in outline, and is surrounded by a wide gray zone containing a

few punctate hæmorrhagic areas. The tumor tissue shades off very gradually into the softened brain tissue.

In the right island of Reil is another smaller tumor, more regular in outline, measuring 1 cm. in outline. This tumor extends to the corpus striatum, but does not involve it. It is surrounded by a firm connective tissue capsule. Its center is made up of soft caseous material. The grayish peripheral zone of this tumor is very narrow. The ependyma of the upper third of the floor of the fourth ventricle and the entire aqueduct of Sylvius is ragged and covered with clotted blood. No tumor mass could be detected in this vicinity, and sections through the pons do not reveal gross lesions aside from the softening of the ependyma and the tissue immediately subjacent. Small hemorrhagic areas are found scattered throughout the pons.

The cord shows no gross lesions—it is preserved in Mueller's fluid.

Specimens for microscopic sections were removed from the tumors and from the softened brain tissue beneath the ependyma of the descending horn of left ventricle.

Microscopic examination of the tumor tissue shows that the center of the tumor is made up of numerous areas containing only granular amorphous material. Near the outer zone of the caseous center these necrotic areas are small and scattered, and numerous areas of round-cell infiltration separate them from each other. In the outer, more cellular zone there are a few small scattered tubercles. Giant cells are found in the periphery of the necrotic area; are more common, however, in the areas of perivascular infiltration. The softened cortex in the vicinity of the tumor has lost its characteristic histological structure. The pyramidal cells are sparse, the cell body stains only very faintly and the nucleus in many of the cells has entirely disappeared; in others it takes the stain but very faintly. The protoplasmic processes that can be traced for some little distance in the healthy cortex when thionin or methylene-blue is employed, are not visible here. A nucleolus is visible in a few of the pyramidal cells in the preparation stained with thionin. The preparations made from the tumor in the right island of Reil show a very dense connective tissue band surrounding the entirely necrotic center.

Here and there cystic cavities appear in the tumor tissue (tip of left temporal lobe) that appear to be enormously distended perivascular spaces. Nearly all the vessels, but more particularly those in the periphery of the tumor, are enormously thickened. There is a marked proliferation of the endothelium, the muscularis is studded with round cells, and in many vessels there is an enormous zone of round-cell infiltration and connective tissue proliferation between the muscularis and external elastic lamina, and another zone between this lamina

and the adventitia. Even the central necrotic zones contain some blood vessels, but they are few and their entire wall, save the endothelial layer, seems to have been destroyed. In some of the vessels there is a faint indication of a pre-existing vessel wall, but in others even the intima has been destroyed and groups of red blood cells and pigment are found here and there throughout the necrotic material.

Many sections were stained with carbol fuchsin and searched carefully for tubercle bacilli, but none was demonstrated. Failure to demonstrate the bacilli of tuberculosis leaves some doubt as to the diagnosis of tubercle in this case.

From the histological structure per se it is impossible to differentiate between tuberculous and gummatous new growths; further evidence, however, favors the diagnosis of tubercle. According to Virchow[4] gummatous new growths have the following characteristics: They are angular, nodulated, with an uneven surface; are frequently in connection with the dura mater; are usually surrounded by a broad zone of gelatinous substance, and are not prone to undergo softening. Gummata are very rarely found deep in the brain substance, are usually multiple, and the meninges in the neighborhood almost always show syphilitic thickening. Birch-Hirschfeld[5] states that syphilomata often invade the dura mater and the cerebral substance from the leptomeninges. The dura mater is often thickened and adherent to the skull and leptomeninges, and this is especially true when the tumor is developed on the convexity. The possibility of the development, primarily, of a gumma in the brain substance must be considered, but it is certainly a very rare occurrence. It is conceded by most authorities that giant cells are found in gummata, as well as in tubercles. Oppenheim[2] quotes Baumgarten as authority for the statement that the presence of giant cells in a supposed gumma is indicative of a mixed infection with the tubercle bacillus or a mistake in diagnosis. Many authorities are of the opinion that the tubercle also is apt to have its origin in the meninges and to involve the brain structure secondarily,

but all agree that it is by no means rare to find tubercles deep in the brain structure, where there can be no possibility of an extension from the meninges.

Attention has been called to various histological differences in tubercle and gumma, but they are too slight to enable us to use them for differentiation in every case. It is possible that by a careful and detailed consideration of a given granulation tumor we may come to a reliable conclusion. In tubercle, after caseation occurs, it is apt to involve the entire center, and only the more or less regular peripheral zone contains living tissue. In gumma the caseous area is often traversed by bands of granulation tissue. Suppuration very rarely or never occurs in gummata. According to E. Klebs[6] the intercellular framework is much better developed in syphilomata. Even after a syphiloma becomes caseous it is much firmer than is the case in tubercle. Bruns[1] states that gummata are often surrounded by much cicatricial tissue and contain many sclerotic vessels. Tubercles are more apt to be surrounded by a zone of softened tissue. Klebs, Oppenheim and Bruns agree that the giant cell is essentially a product of tuberculosis. They refer to the cell made up of a homogeneous, hyaline-like protoplasm with one or more rows of oval nuclei at the periphery. Thickened vessels are found more frequently in gummata, but it is by no means rare to find them in tubercles. In the case under discussion there was no evidence of tuberculosis or syphilis in the other organs and no history of syphilis was obtained.

A careful examination of sections of the spinal cord stained after Weigert's hæmatoxylin and Marchi's methods fails to reveal a posterior column sclerosis. This is an interesting feature in this case because of the controversy that has arisen over the not infrequent combination of tabes dorsalis with brain tumors. Oppenheim[2] has observed a case in which there were symptoms that pointed to the coexistence of tabes dorsalis and brain tu-

mor, and later demonstrated a typical posterior column degeneration. Knapp, Mendel, Drummond, Taylor, Handford, Coxwell and others have reported cases of this kind. C. Mayer and Dinkler have attributed the posterior column sclerosis to the pressure of the enormously increased cerebro-spinal fluid. In our case there was absence of the knee-jerk, a marked ataxia and reflex iridoplegia, which would very naturally lead one to think of a tabes dorsalis. Absence of the knee-jerk has been noted in cases of brain tumor in which no posterior column disease could be demonstrated. Ataxia has frequently been observed in bulbar lesions. In many of these cases it seems probable that the cerebellum or its peduncles were compressed, but there can be no doubt that lesions of the medulla or pons may, without compression of the cerebellum or its peduncles, give rise to a genuine ataxia of the cerebellar type.

Case 3.—A. T., female, age 32, was admitted Sept. 22, 1897, with the history that she had an epileptic seizure in December, 1896, several in January and February, 1897. These seizures are said to have occurred during the menstrual period. Prior to her first epileptic seizure she was considered normal mentally and physically, although she had, for a year or more previously, often remarked that she feared she would become insane. She had been suffering from intense frontal headache, much aggravated at the menstrual periods. Since December, 1896, she has very gradually become indifferent, forgetful, has urinated and defecated involuntarily. Her speech is slow and hesitating. There is considerable muscular weakness and a marked ataxia. Right pupil wider than left; double choked disc; vision fairly good. Oct. 9, 1897, the patient had two general epileptic convulsions, followed by stupor. Gait became very slow, with a tendency to drag the feet. There was marked tremor of the hands. Knee-jerk very active. The mental dullness steadily became more marked. At 10 p.m., October 11, profuse vomiting followed by deep coma, which persisted until her death at 6:10 a.m., October 12.

The necropsy record is without interest, except for the findings in the brain. The calvarium is perfectly symmetrical; the sutures and other markings are normal. The frontal bones are relatively thick—6 mm., while the occipital measures but 3 mm. The dura mater is very tense and dry. The markings on the convexity of the brain, especially in the frontal region, are almost

entirely obliterated; the leptomeninges are dry. The right hemisphere, in the region of the gyrus fornicatus, bulges and has made a large indenture in the corresponding area of the left hemisphere. The anterior half of the corpus callosum is enlarged, of irregular outline and much firmer than is normal. The right frontal lobe is of greater volume and much firmer than the left. The entire right frontal, anterior portion of right parietal and the corpus callosum are transformed into a tumor mass, which, in the right parietal and posterior portion of frontal lobes, contains many larger and smaller cystic cavities and gelatinous areas of softening, while in the anterior portion of the frontal lobe and the corpus callosum the consistence is decidedly increased. The right corpus striatum is also slightly involved. The optic nerves and posterior half of each eye were removed. The discs were much swollen, their peripheries indistinct, and many hemorrhagic streaks were visible in the fundus. Pieces of tissue from various areas of the tumor were fixed in formalin, hardened in alcohols of increasing strength, cleared in toluol and imbedded in paraffin. Sections of this material were stained with formalin-saffranin, hæmatoxylin and eosin, thionin, methylene blue, nuclear black and after Van Giesen's method.

Microscopic examination of these sections showed an illy defined fibrillar network, containing numerous nuclei, some of which are apparently free; others are surrounded by a narrow, indistinct zone of homogeneous protoplasm. Aside from these there are a great many more or less irregular homogeneous, faintly stained, hyaline-like bodies, some of which contain a well-stained nucleus which seems crowded to the very periphery and in many instances is much flattened. Occasionally a body of this kind is found with a faintly stained and more or less centrally located nucleus. A large portion of these bodies is apparently without a nucleus. The large homogeneous cell bodies are found in all portions of the tumor, even in the softened areas, but are closely packed in the corpus callosum. Surrounding these free nuclei and large cell bodies is a sparse fibrillar framework.

It is difficult or impossible to decide definitely as to the nature of these large homogeneous bodies after this very ordinary process of staining. To enable us to do this small pieces of tissue, having been thoroughly fixed

in formalin, were treated after the method of Mallory[7], the steps of which we briefly outline here:

1. Formalin, 10 per cent. aqueous sol., 4 days or longer.

2. Picric acid, sat. aqueous sol., 4-8 days. Steps 1 and 2 may be combined.

3. Ammonium bichromate, 5 per cent. aqueous sol., in incubator at 37° C. for 4-6 days. Change sol. on second day.

4. Dehydrate in alcohol without first washing in water.

5. Imbed in celloiden. (Our material was imbedded in paraffin.)

Sections of tissues mordanted in this way were stained after Weigert's fibrin stain, slightly modified by Mallory; others with Mallory's phospho-tungstic acid, hæmatoxylin, methyl-violet, methylene-blue, thionin, etc.

The large homogeneous bodies referred to above are beautifully stained by the methyl-violet and also by the phospho-tungstic acid hæmatoxylin.

In the majority of those which, after the ordinary staining, appear to be without a nucleus, one or two faintly stained nuclei are brought out. The single nuclei are usually at one pole of the cell, though in many cells they are found near the center. One unmistakable mitotic figure is present in a preparation stained with methyl-violet after Mallory's mordant had been used. The bodies are seen to be much more irregular than they appeared in the unmordanted tissues and from one to six processes can be demonstrated on many of them. Many fibers, identical in appearance with the ganglion cell process are seen among the cells, but they do not appear to be directly connected with them. They are not so numerous but that they can be looked upon as processes of some cell body. It can scarcely be denied, however, that they may be free fibers, in the sense that they have no cell connection.

In this case the diagnosis of neuroglioma ganglionare seems justifiable in view of the occurrence, in the tumor tissue, of the well- developed fibrillar network, the large nucleated ganglion cells and the smaller cells, some of which contain a small zone of perinuclear protoplasm, whereas in others nothing but a nucleus is to be seen.

There has been much confusion in the discussion of this specific tumor of the central nervous system. It has been and is still confounded with sarcoma so much that it is impossible to decide, from descriptions of the microscopic findings in the majority of the cases found in the literature, whether a given case was one of glioma or sarcoma; in fact, in many of the cases the tumor has been designated glio-sarcoma.

Since, His, Von Lenhossèk and others pointed out to us the epiblastic origin of the glia cells these elements have been subjected to more careful histological and pathological study and much has been done in the differentiation of glioma and sarcoma.

It must not be denied that gliomatous and sarcomatous elements may be found in the same growth, but this is certainly a very rare occurrence.

Strœbe[8] and Ziegler[9] agree that the term glio-sarcoma should be limited to gliomata, in which there is an actual neoplastic proliferation of mesoblastic tissue in addition to the epiblastic growth, and that this mesoblastic proliferation must have its origin in the vessels of their sheaths. Microscopic differentiation has been attempted on the basis of the richness or paucity of the cellular elements. In many cases found in the literature it seems that a diagnosis of sarcoma or glio-sarcoma has been made because the cellular elements were numerous. Thoma[10] recognizes the epiblastic origin of glia tissue but still believes that a glioma is capable of development into a rapidly growing glio-sarcoma. Allen Starr[11] and Oppenheim[2] as well as Bruns[1] use the term glio-sarcoma,

although Bruns is of the opinion that gliomata are to from sarcoma. Differentiation has also been attempted on the basis that the cells in gliomata are always surrounded by a zone of protoplasm with many branches. This branching protoplasm can often be demonstrated only in the fresh, teased preparation, but undoubted gliomata do occur in which many of the cells are devoid of this protoplasm. In preparations of gliomatous tissue mordanted in Mallory's or Weigert's fluid for the special purpose of bringing out the protoplasm of the cell-body and its branches, many free nuclei are found.

Neuroglioma ganglionare is, according to E. Klebs, a new growth in which true nerve elements as well as glia tissue proliferate. Oppenheim[2] gives an illustration borrowed from Zeigler in which these elements are beautifully shown. The ganglion cells in this figure are somewhat more regular, their protoplasm is granular and the nucleus is usually found near the center of the cell. Many deeply stained fibers are depicted, which are looked upon as true nerve fibers. In those of our preparations that were stained with Weigert's hæmatoxylin many deeply stained fibers are present, but they are more numerous and vary much in size. It seems to us impossible to decide definitely upon these as being nerve fibers in spite of the fact that Weigert's stain was employed.

Professor E. Klebs of Chicago has very kindly made a careful examination of our preparations and states very positively that this tumor is to be classed with what he has described, as quoted by Oppenheim, Birch-Hirschfeld and others, as neuroglioma ganglionare.

Many authors, including Osler, do not consider the ganglion cells and so-called nerve fibers that are found in the neuroglioma ganglionare to be genuine nerve elements. Raymond and some others consider that some of this glia cell as the "Ersatzzelle." Other observers, glia cells are capable, under the proper stimulus, of

transformation to genuine nerve cells. Raymond speaks on the other hand, insist that these ganglion cells and nerve fibers can only be derived from pre-existing nerve cells.

Our preparations do not permit us to add anything to the much discussed question of the disassociation of glia fibers. Taylor[12] in his very able article of recent date takes up this question of the disassociation of glia fibers and comes to the conclusion that "the development of neuroglia in all probability is from cells with protoplasmic processes to cells with differentiated and independent fibers," and also that "the term glio-sarcoma should be dropped as unscientific and misleading in its significance. No criterion has yet been offered to determine a fundamental distinction between glioma and sarcoma (Strœbe) and secondly between glioma and so-called gliosis (Weigert)."

Mental disturbances in cases of brain tumor are the rule, although in many cases they are slight. The increase of the intercranial pressure is the usual cause of the psychic changes, but in many cases it must be admitted that the particular location of the tumor is largely responsible. Tumors of considerable size may develop in the so-called silent areas without giving rise to mental changes other than a more or less marked loss of memory, but as soon as the intercranial pressure increases materially there develops a confusion and what may be termed a mental asthenia. Great effort is necessary to concentrate the attention and sometimes this can be brought about only with the more powerful stimuli, and then but for a short time, as though the least mental effort were followed by great exhaustion. Reasoning and memory are almost always impaired, at times to a very marked degree. Occasionally a melancholic condition is the only sign of mental impairment. Oppenheim[2] reports a case in which a choked disc and a mental condition not to be differentiated from the ordinary

melancholia were the only symptoms of brain tumor. Not infrequently attacks of maniacal excitement, hallucinatory confusion or actual delirium have been observed. Rarely do we meet with paranoia-like symptoms. One case of this kind was observed by Dinkler.

It is important to note that psychical disturbances may constitute the earliest symptoms of brain tumor. Wollenberg cites the case of a woman who was admitted to the hospital with a diagnosis of hallucinatory delirium. Some time later she was readmitted with other symptoms of brain tumor. In Oppenheim's cases the earliest mental symptoms were usually those of mere indisposition and apathy. As the tumor develops there ensues a progressive dementia, with or without paralysis. Kraepelin[14] speaks of the frequently recurring periods of excitement, the psycho-epileptic seizures. Occasionally a cataleptic state has been noted and a very stupid condition with a tendency to much sleep. Delusions, illusions and hallucinations are uncommon and are said to be most apt to occur in cerebellar tumors. Visual and auditory hallucinations have been noted in completely blind and deaf individuals. Hughlings Jackson has reported a case of tumor of the temporal lobe with hallucinations of smell. Leubuscher[15] in his work on diseases of the brain published in 1854 says of the psychical symptoms of brain tumors that they are usually not very marked and for that reason comparatively few cases are admitted to asylums. In 350 necropsies made by him in asylums he met with but four cases of brain tumor, one tubercle, one cysticercus and two cancers. Leubuscher met with many cases of brain tumor in which there was mental impairment, and speaks of maniacal attacks, loss of memory, confusion and dementia. Coma often precedes death.

A much-discussed question in brain physiology is the function of the frontal lobes. Many observers believe that tumors of the frontal lobes, other things being equal,

are no more apt to give rise to psychic changes than those in other portions of the encephalon. Even the more recently reported cases leave us much in doubt as to the relation of the frontal lobes to the higher psychic functions, but they demonstrate quite satisfactorily that in the great majority of the well-observed cases of tumors of the frontal lobes there is early impairment of the psychic functions or a decided psychosis. Ferrier, Starr, Knapp and others are inclined to look upon marked mental aberration occurring early in a case of brain tumor as a focal symptom of disease of the frontal lobes. It is probable that disease of the left frontal lobe is no more apt to give rise to mental impairment than is disease of the right except for the frequent combination of psychic deterioration with the symptom-complex aphasia.

The nature of the tumor has little or no effect upon the mental changes, although it has been contended that the cysticercus cerebri is unusually apt to give rise to psychic disorder. The probable explanation is the frequent multiplicity of the growths. Jastrowitz[16] says: "A certain form of mental disturbance, a form of dementia with characteristic excitement, the so-called moria, I have observed only in tumors of the frontal lobes." He says of one of his patients that he was good-natured, confused and mentally weak. Occasionally there was a marked tendency to coarse joking. Often there is a certain humorous tendency in their speech and general behavior which makes them appear very comical and this comical tendency is often in direct contrast to the otherwise apathetic and amnesic condition of the mind. Jastrowitz cites another case of tumor of a frontal lobe in a man who, in his very demented and confused condition, made sarcastic and comical remarks to and about those around him. In still another case a patient answered in a short, sarcastic manner, making at the same time all sorts of grimaces. Later

Jastrowitz concluded that moria was found only in a portion of the cases of frontal tumor and that it was sometimes found in frontal lesions other than tumor. In some cases of senile dementia, in general paresis and in alcoholics, moria has been observed and Jastrowitz has claimed that even in these conditions the moria was significant of frontal lobe disease.

It is to be remembered that such coarse brain diseases as tumors are sometimes complicated with hysteria and in these cases the symptoms of hysteria are not to be confounded with those of the tumor.

LITERATURE.

1. Bruns, L.: Die Geschwülste des Nervensystems. Berlin, 1897.
2. Oppenheim: Die Geschwülste des Gehirns. Nothnagel's Specielle Path. und Ther., Band ix, Abtheilung iii, 1st ed.
3. Bristow: Brain, October, 1884.
4. Virchow: Die Krankhafte Geschwülste.
5. Birch-Hirschfeld: Lehrbuch der Path. Anat., Band i, Spec. Theil,, p. 335.
6. Klebs, E.: Allegemeine Pathologie, ii, 3.
7. Mallory, F. B.; Journal of Experimental Medicine, vol. ii, p. 532.
8. Stroebe: Ueber Entstehung und Bau der Gehirngliome. Zeigler's Beiträge, xviii, 895; Centralblatt für allg. Path. und Anatomie, vii, 896.
9. Ziegler: Lehrbuch der Path. Anatomie, Band ii, p. 332.
10. Thoma: Lehrbuch der Path. Anatomie, Theil i, pp. 661 to 663, 1894.
11. Allen Starr: Brain Surgery, 1893.
12. E. W. Taylor: A Contribution to the Study of Human Neuroglia Journal of Experimental Medicine, vol. ii, p. 611.
13. Ziemssen: Cyclopedia of the Practice of Medicine, vol. xii, p. 245.
14. Kaepelin: Psychiatrie, 1896, p. 20.
15. Leurbusher: Gehirnkrankheiten, 1854.
16. Jcastrowitz: Verhandlungen des Vereins für innere Medicin, Berlin 1886.

D. N. Eisendrath read a paper upon the pathology of epidemic cerebrospinal meningitis, February 13, 1899.

Alice Hamilton reported a case of tumor of the brain, showing a peculiar form of degeneration, March 13, 1899.

THE EYE

THE CHARACTER OF THE CELLULAR EXUDATION IN ACUTE KERATITIS OF THE RABBIT.

W. T. COUNCILMAN.

Those changes in tissue which follow an injury, and which in their entirety we call inflammation, have long been a favorite subject both for investigation and for theory. Almost all the old systems of medicine, based as they were on theoretical conceptions of disease, used the inflammatory processes to furnish proof of the correctness of the particular theory set forth. The real investigation of the inflammatory changes may be said to have begun with John Hunter. Hunter, Waller, Virchow, and Cohnheim are the names with which the great advances in our knowledge of the process have been associated. Ehrlich has indirectly contributed much in teaching the differences in the character of the leucocytes, and giving us methods by which they may be distinguished with more or less accuracy. The very slight contribution to our knowledge of the subject which I shall offer you tonight is the result of the study of a subject pursued very intermittently.

The cornea has been and must for some time remain a favorite tissue for experimental investigation for the pathologist. A review of all the articles written in the last forty years on acute inflammation of the cornea would carry us over the entire history of the various theories on the origin of the new cells in inflamed tissue. Whatever theory was advanced, its upholders have found

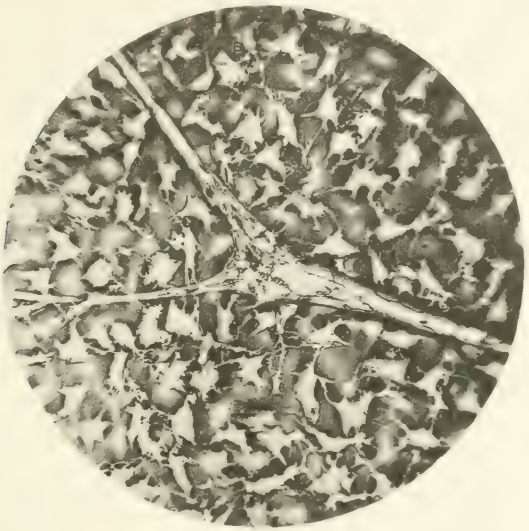


Fig. 1.

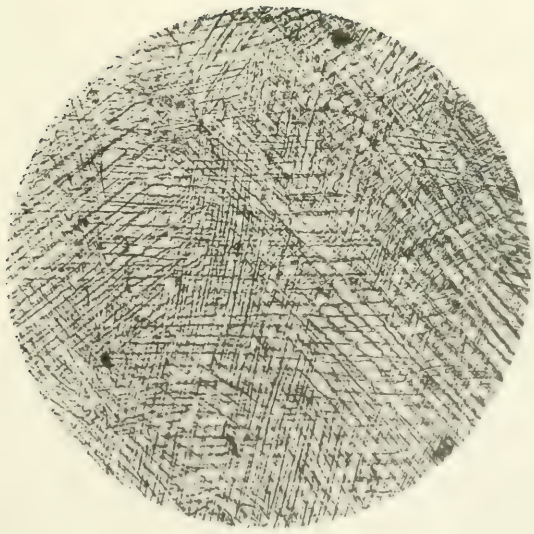


Fig. 2.

COUNCILMAN & LEBARON

support in what they found in this tissue. The illustrations which form a part of the numerous articles would fill a large volume. They are in part objective, with the author's interpretations added to the objective features, and in part imaginary. The reason that the cornea has been so generally selected for the study of inflammation lies in the great simplicity of the tissue and the absence of blood-vessels. We know definitely the character of the cells which are normally present in the tissue, and knowing this it should be easy to determine the character and origin of the numerous new cells which are found in it when inflamed. The tissue is also admirably adapted to the study of the character of the cell changes which are produced in tissue by the various bacteria.

The cornea is covered with several layers of epithelial cells differing neither in character nor arrangement from those covering the conjunctiva. Below the epithelium is the proper tissue of the cornea, which agrees in its general features with the connective tissue. It is made up of straight fibers which give the reaction of white fibrous tissue, and which are arranged in planes. The fibers in these planes run in various directions, usually at right or oblique angles with the fibers in the overlying planes. They are all straight, and all those in the same plane are parallel. Between the fibers there is a general ground substance which stains brown with nitrate of silver. In good nitrate of silver preparations of the cornea these fibers are not visible. In preparations made from edematous corneas, and when the tissue is slightly swollen in acid, the nitrate of silver solution penetrates between the fibers, forming brown lines. The corneal corpuscles are connective tissue cells, flattened antero-posteriorly, which lie between the layers of the fibers.

In a properly prepared specimen stained with nitrate of silver there are numerous clear spaces which have extremely irregular outlines, and which communicate by means of numerous processes with both the spaces on the

same plane and those above and below. After staining the silver specimen with a nuclear stain, large, irregular, pale, or slightly granular nuclei are found in these spaces. Rarely two nuclei are found in the cell spaces. These are the nuclei of the corneal corpuscles, and the protoplasm of these fills the space. In gold preparations, in which all the protoplasm is stained, a protoplasmic network, similar to the network of spaces in the silver cornea is seen.

In addition to the spaces in the tissue occupied by the corneal corpuscles, long spaces are seen which extend from the periphery to the center, constantly dividing into smaller branches. The larger spaces show a tracery of silver lines similar to a lymphatic vessel. In the smaller spaces the lines are more irregular. These are the spaces in which the nerves run, and the corneal spaces open freely into them. The cornea has no blood-vessels or lymphatics, properly speaking, although the nerve channels, representing perineural lymph spaces, take the place of the latter. These nerve channels can be regarded simply as enlarged and elongated cell spaces lined on all sides by flattened corneal corpuscles similar to those in the tissue.

Other cells are found in the tissue in addition to the corneal corpuscles. In places an elongated protoplasmic thread resembling a nerve, but differing from this in the presence of a nucleus similarly elongated, is found in the tissue. These cells may be so outstretched as to extend entirely across the field of the microscope, and are parallel to the corneal fibers in the same plane. Or a round cell, with a curved irregular nucleus, is found in the same cell space, with a corneal corpuscle, or in the irregular space between two corneal spaces, conforming itself to the shape of this. These cells are most numerous in the upper layers of the tissue, and near the scleral margin. On an average not more than eight or twelve will be found in a thin section of the entire cornea.

These are the wandering cells of the tissue described by Recklinghausen many years ago.

So much for the normal tissue. Inflammation may be produced in the tissue in a variety of ways, and the changes produced are alike in their general features, though they differ somewhat according to the degree of the inflammation and the character of the agent used to produce it.

From the many articles which have been written on this subject, though there are some contradictions, we can accept the following: In the inflamed cornea numerous new cells appear. These cells are leucocytes which emigrate from the vessels of the sclera and conjunctiva, and make their way to the point of irritation. In part they pass to this through the corneal tissue, either by means of the cell spaces, passing from space to space through the communicating channels, or they take a more direct route between the fibers. When in the cell spaces they retain their round form, when between the fibers they are elongated, but not so much so as in the same place in the normal. This is due to the fact that the tissue is edematous and the fibers are somewhat separated by the fluid between them. Comparatively few cells reach the center by this route. Most of those found there come more directly. In the normal fluid of the conjunctiva a few leucocytes will be found, in addition to desquamated epithelial cells. If the fluid be examined a few minutes after inoculating the center of the cornea numbers of leucocytes are found. These pass not into the corneal tissue after emigration, but directly through the conjunctival membrane into the sac, and from here into the wound made in the center. They are attracted to the center by the mysterious quality termed chemotaxis, the attraction being exercised by the exciting agent, by the necrotic tissue, or both.

The number of leucocytes and their situation in the tissue vary enormously in the different sorts of inflamma-

tion. They are most numerous in the acute inflammation produced by inoculation with the staphylococcus. Their presence in the central lesion is facilitated by an opening in the tissue by means of which they can enter. It is possible by various means to produce a limited necrosis of the tissue without any lesion of continuity, and in these cases the infiltration around the lesion may be entirely absent. Leucocytes will, however, always be found in varying numbers around the periphery.

The corneal corpuscles take no part in the production of these cells. They proliferate, but the resulting cells are new corneal corpuscles which take the place of those which have been destroyed. In exciting an inflammation in the tissue the corneal corpuscles immediately acted on are destroyed, and the proliferating cells are confined to the small area surrounding the corpuscles thus destroyed.

My experiments on the cornea have been made mainly with the view of determining more closely the various steps in the process, and the part played by the different leucocytes found in the blood.

Rabbits were used almost exclusively for the experiments, and the eye inflamed after a local anesthesia was produced by cocain, or general anesthesia by ether. With few exceptions a more intense inflammation followed a lesion of the same character when cocain was used. For producing inflammation a pure culture of a virulent staphylococcus was used, the inoculation being made by scratching the center of the cornea with a knife on the point of which a small amount of the pure culture was placed. The animal was killed and the eyes examined after intervals of 6, 8, 12, 18, 24, 36 and 48 hours, and daily up to the thirteenth day

For studying the aseptic inflammations nitrate of silver, caustic potash, and chlorid of zinc were used as irritants, and the eyes examined after varying intervals. Usually there is difficulty in confining the lesion produced by caustic potash to a small extent of surface, but

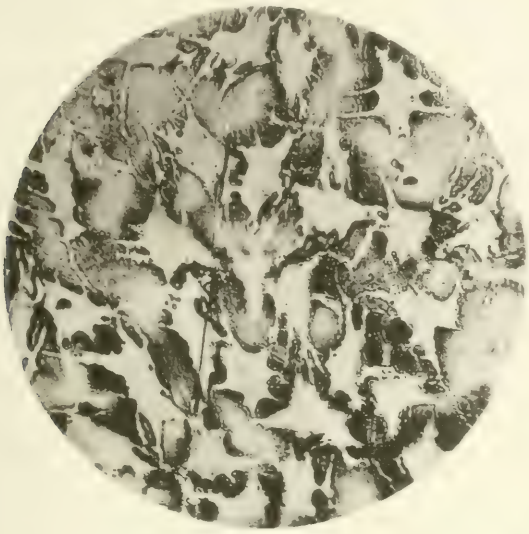


Fig. 1

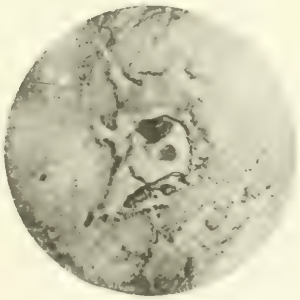


Fig. 2

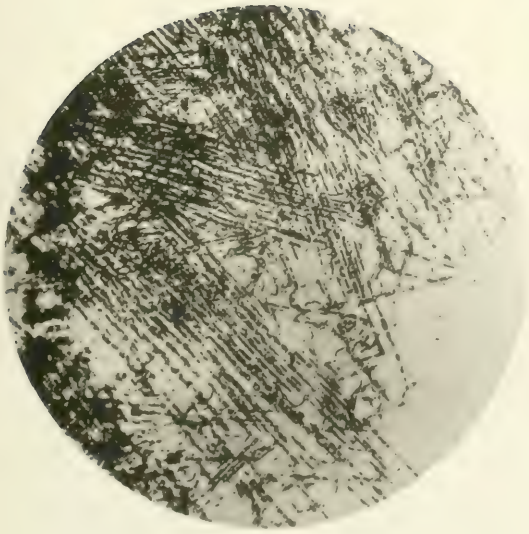


Fig. 3

this was overcome by the use of a fine glass tube filled loosely with absorbent cotton, which was cut off flush with the end of the tube. The cotton was moistened with a saturated solution of the caustic, and the end of the tube placed in contact with the surface.

The tissue was examined in the fresh state after staining with nitrate of silver, or after hardening in Zenker's fluid or corrosive sublimate alone. For the silver method the animal is anesthetized and the cornea thoroughly rubbed with a crystal of the silver, an attempt being made in this way to remove the surface epithelium. The animal is kept anesthetized for ten minutes, after which it is killed. The cornea at once takes on a dull grayish appearance, and a whitish precipitate appears in the anterior chamber. The eye is then enucleated and washed for ten minutes in running water, after which the cornea, with a part of the scleral margin, is removed and exposed to the action of diffuse daylight, in a mixture of glycerin and water to which a couple of drops of acetic acid have been added. In twenty-four hours the tissue has become brown and is slightly swollen. Four incisions in the shape of a maltese cross, extending from the periphery almost to the center, are made in it, and it is cut into thin sections by the freezing microtome. There is no difficulty in making twenty to thirty sections, taking in the entire extent of the cornea. The excellence of the sections depends upon the sharpness of the knife and the proper degree of hardness produced in freezing.

The sections are washed in water until all trace of the acid has disappeared, stained in hematoxylin, and mounted in balsam. The mounting should be done entirely on the slide. The sections are removed from the water, spread out on the slide, and treated with 80 per cent. alcohol, aniline oil, xylol and balsam, the sections being blotted between the use of each reagent.

In many cases one eye was treated with silver and the

other hardened and cut after embedding in paraffine. Both of these methods of preparation are necessary for the study of all the steps of the process. Each has certain advantages over the other. The situation of the leucocytes in the tissue is best seen in the silver preparations. The nuclear figures in the dividing corpuscles are also preserved in a remarkable manner in this way. The form and character of the leucocytes is best shown after hardening in Zenker's fluid or sublimate. It would carry us too much into detail to attempt a description of the various stages of the inflammations so produced, and I shall only attempt to give you the general features of the process. This will include:

1. The character of the leucocytes which emigrate.
2. From what vessels they come.
3. What changes they undergo in the course of their migration.
4. What changes take place in the corneal corpuscles.
5. Under what conditions, and how, does the new formation of blood-vessels take place.

From a study of the rabbit's blood and of inflammation in various parts of the body produced in various ways we can conclude that there are three distinct varieties of leucocytes which emigrate and take part in the inflammatory process: First, the leucocytes, which I shall speak of as the granular leucocytes, and which correspond to the polymorphonuclear leucocytes in human blood. These leucocytes have a nucleus composed of several more or less irregular fragments which are all united by slight filaments of nuclear material. The nucleus stains intensely with all sorts of staining reagents, having about the same degree of affinity for color as has the chromatin of a nuclear figure. The nucleus is homogeneous, and no structure can be distinguished in it. The protoplasm is granular, the granules round, of equal size, and they stain intensely with eosin. Around the cell there is a perfectly distinct, dense, limiting mem-

brane which is brought out sharply in corneas stained with Mallory's phosphotungstic acid hematoxylin. This limiting membrane is one of the most distinct features of the cell, and is more marked in these cells than in any others in the body.

The second variety I shall designate as the non-granular leucocytes. These are about the same size as the first named. The nucleus is usually elongated and curved in various degrees. Often it has the definite form of a horse-shoe. It is never divided into small masses as is the first named. It does not stain so intensely, and is more or less granular. The periphery is colored more intensely than the center. The protoplasm is slightly granular, but the granules have no definite size and no special staining affinity. There is no cell membrane giving a sharp outline to the cell as in the granular leucocytes.

The third variety is the lymphocyte. This is much smaller than the first two, and has a perfectly characteristic nucleus. The nucleus is round, the periphery stains sharply, and small masses of chromatin project from the periphery and are connected by chromatin threads with similar granules in the interior, giving the nucleus a granular, reticular appearance, even under low power. There is no cell membrane, and only a very small rim of homogeneous protoplasm can be distinguished around the nucleus. Often even this small amount seems to be absent.

All these leucocytes emigrate. The numbers of each found in the tissue vary with the character of the inflammation, its intensity, and the time which has elapsed since the infliction of the injury. The granular leucocyte is by far the most active in the emigration. It is found in greatest numbers, it is the first to emigrate, and in the early stages of inflammation it may be found alone. In the normal cornea this leucocyte is the only one found in the tissue. It is found also in the tissue of

the normal mesentery, and seems to be the only form of wandering leucocyte in normal tissues. Fifteen minutes after inoculating the center of the cornea with the staphylococcus these cells are found in considerable numbers in the tissue of the conjunctiva. They pass from the vessels by means of their ameboid motion and at once begin their process toward the center. In passing through the corneal tissue they seem to travel by preference through the fibers. Their motion, as far as can be judged by the examination of the specimens which have been instantly set by the hardening fluid, is similar to that of an ameba. They become easily broken up and destroyed. Observing a cornea containing a number of them, one is struck by the presence of small round masses in their vicinity. These masses are of various sizes, and contain a varying number of granules similar to those in the cell. Occasionally a corpuscle between the fibers seems to leave behind a trail of these small fragments—occasionally the entire cell fragments. Both nucleus and protoplasm break up into a number of smaller and larger fragments. Between the fibers, even when drawn out into a long filament, which is sometimes so long as to stretch across the field of an immersion lens, the particles of the nucleus are not separated, but remain connected by a filament, often so thin as to be visible only under an immersion.

In the process of migration the nucleus is always directed toward the objective point, and in migrating from a vessel the nucleus with a small mass of protoplasm passes through first. These cells in part pass through the cornea; in part they take a much more direct route to the center by means of the conjunctival sac. Even in the cornea they are found in much greater numbers in the upper layers and are constantly passing from here to the surface through the epithelium. In the early stages of inflammation all the leucocytes found around the center are composed of this variety. In the center they

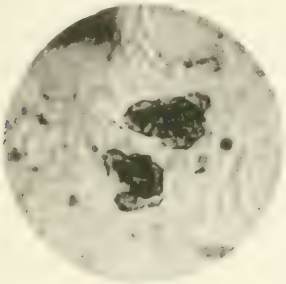


Fig. 2.

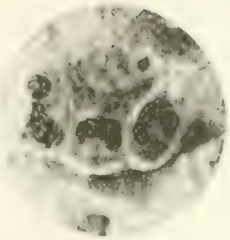


Fig. 9.

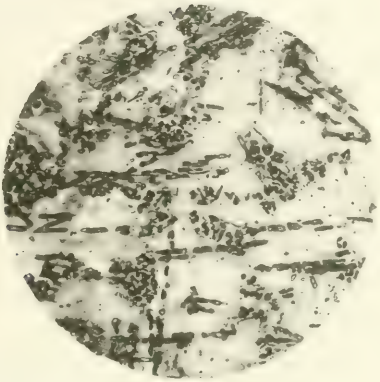


Fig. 1.

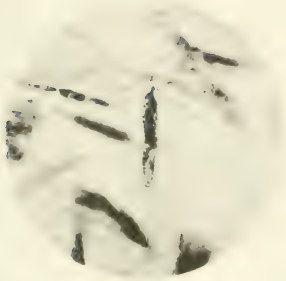


Fig. 4.

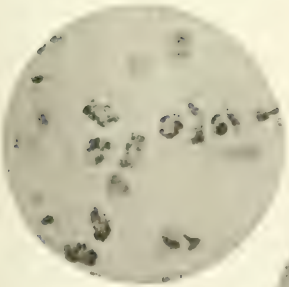


Fig. 8.

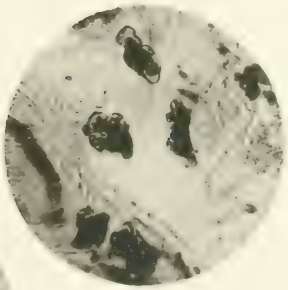


Fig. 3.

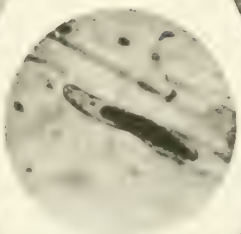


Fig. 5.

Fig. 6.

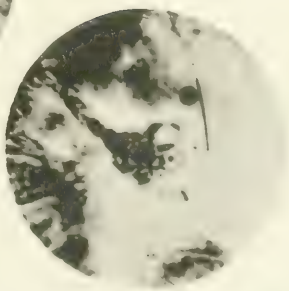


Fig. 7.

are so closely packed that their situation is obscured, but on the edge of the mass it is evident that they are between the fibers. They undergo such rapid fragmentation here that in places only a granular mass of cell and nuclear fragments can be made out.

The second variety, the non-granular leucocytes, vary extremely in number. They are most numerous in corneas examined 18 to 24 hours after inoculation. In the tissue they are most frequently found in the cell spaces, though not confined to this situation. It is always easy to distinguish them from the others. Between the fibers they are usually pointed at both ends, the nucleus being in the middle. They are numerous in the cell spaces in the periphery; they do not seem to pass into the conjunctival sac to any considerable distance, and I have not found them in the central lesion. Their motion is slow; they are not found in the irregular forms with knob-like prolongations which are characteristic in the first.

The third form of wandering cell found in the tissue is the lymphocyte. Probably only a small part of these come from the vessels, and their emigration is rarely seen. They do not appear in the corneal tissue before the fourth day, and then are usually found only in the cell spaces around the periphery. I have never found them between the fibers. It is probable that they have some feeble power of ameboid motion, for they have been seen in the act of passing through the wall of a vessel, and are also found in shapes strongly suggestive of this. When the tissue is being vascularized they are frequently seen in the vicinity of the newly-formed vessels. Their presence in the cornea is only partly to be accounted for by active emigration. Probably the most potent factor in bringing them there is the increased lymph stream entering the tissue, they being carried along in this just as are the red corpuscles. Red blood corpuscles are found in considerable numbers in the periphery of the

cornea forty-eight hours after an intense inflammation has been produced by the staphylococcus inoculation. Most of the lymphocytes come from the mass of lymphatic tissue found around the vessels outside of the cornea. The normal tissue here contains great numbers of these cells, and the inflamed tissue is so packed with them as to suggest a section of a lymphatic gland. They are added to slightly by emigration, the increase being principally due to multiplication of the existing cells. Evidence of this multiplication is found in the presence of numerous clear figures. The division of the cells always takes place by mitosis, and not, as has been assumed by some, by direct division.

In studying sections of corneas five days or more after central injury, cells are found which do not correspond with any of those mentioned, and it was only after studying inflammation in other tissues that their character became plain. They are only found in the outer third of the cornea, never around the central injury. They are both in the cell spaces and in the tissue between the fibers. These cells are as large as the granular leucocytes; the nucleus is round or oval, with the characteristics of the lymphoid nucleus; the protoplasm is dense, non-granular, and stains deeply. Similar cells are found in the tissue of the conjunctiva, and among the lymphoid cells around the vessels.

The study of inflammation in various tissues has enabled me to recognize these as plasma cells. They are formed from the lymphoid cells by the gradual formation of protoplasm around the nucleus. They are more actively ameboid than are the lymphocytes, as their presence between the corneal fibers shows, but they are never so active as the granular leucocytes. Cells showing every gradation between lymphoid and plasma cells are found in the surrounding tissue, and occasionally in the cornea. The conversion of lymphoid cells into plasma cells prob-

ably takes place in the outside tissue from which they enter the cornea.

The lymphoid cells and their derivatives are the only migrating cells which show any progressive changes. The other leucocytes simply degenerate. I have never found any nuclear figures or other evidences of cell division in them.

In making flat sections of the cornea which include the surrounding conjunctiva and sclera, two sets of vessels will be found. Immediately beneath the conjunctival epithelium and in the loose connective tissue there are numerous fine capillaries. Lower down and immediately outside of the cornea there is a plexus of large veins. These veins are almost cavernous, and have frequent communications with one another. They are surrounded by lymphoid tissue. It is from these vessels that the emigration of leucocytes takes place. One often finds great numbers of leucocytes in the conjunctiva and surrounding the vessels in it, while in the vessels themselves, apparently, a normal circulation is going on. I regard this plexus of vessels around the cornea as principally serving its nutrition, and from them both the emigration and new formation of blood-vessels take place.

Changes in the corneal corpuscles are both regressive and progressive, and in no tissue can such changes in cells be studied to such advantage as in the cornea. In producing inflammation of any form the corneal cells which are acted upon by the irritant are destroyed. When nitrate of silver is used to produce the injury the tissue immediately acted upon is coagulated and destroyed. The silver is precipitated in the ground substance and a dark brown eschar is produced in which the outlines of the cell spaces are distinct. Immediately around the periphery of the eschar the cell spaces are small and contracted, and on staining the tissue with hematoxylin an irregular, contracted nucleus, or often fragments of the nucleus, is seen in the space. Farther out in the tis-

sue another form of degeneration is seen. The protoplasm of the cell is broken up into a great number of larger and smaller fragments which are marked off by silver lines between them. The chromatin of the nucleus separates out and forms a number of small crescentic shaped or round masses which are arranged both around the periphery and within the nucleus, the remainder being perfectly clear. The form of the nucleus changes, it becomes large, more irregular in shape, and a central depression appears on each side. The masses of chromatin separate and become arranged in about equal amount in two circles. The constriction increases, the nucleus becomes divided, and two or in some cases three or four such degenerated nuclei are found in a single fragmented cell. This is the direct nuclear division. That it is a regressive and not a progressive change is shown by the fact that no new cell is produced and in the same preparations changes from this to complete fragmentation of both protoplasm and nucleus are found. These peculiar forms of degeneration seem to be more marked in those corneas in which cocain was used as a local anesthetic.

In the eyes in which inflammation was produced by inoculation with staphylococcus aureus the number of leucocytes in the upper layers of the cornea around the center is so great that the regressive changes in the corneal corpuscles are obscured. Lower down we reach an area where neither the leucocytes nor bacteria have penetrated, and in this the cell spaces are irregular and shrunken, and the nuclei of the corneal corpuscles small and angular. This necrotic area, which is always of small extent, is bordered by normal corpuscles, in which, however, there is no sign of activity. Progressive changes in the corneal corpuscles leading to the formation of new corpuscles to take the place of those which have been destroyed are most active in the vicinity of the lesions produced by caustics. The activity of this process varies, and seems to depend upon a number of conditions. It

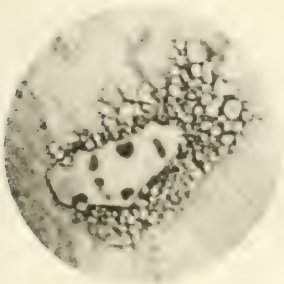


Fig. 2

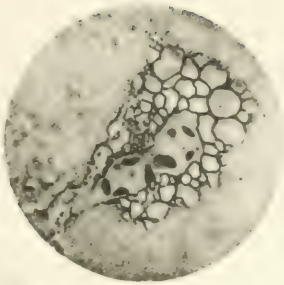


Fig. 3

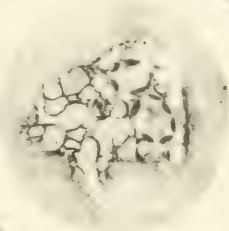


Fig. 4

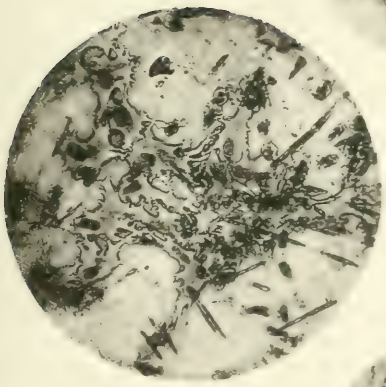


Fig. 5

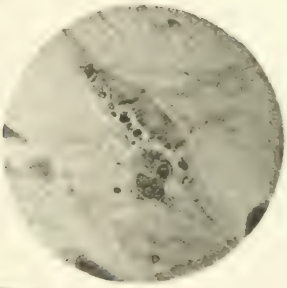


Fig. 1

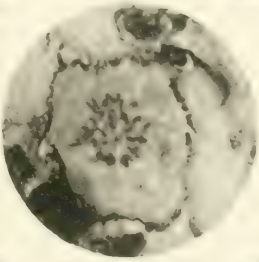


Fig. 6

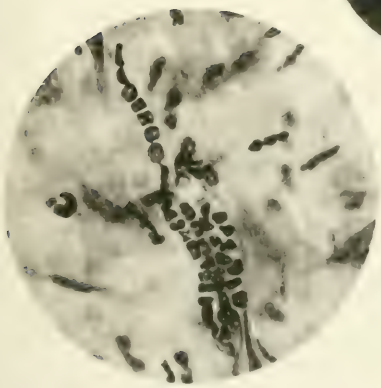


Fig. 8

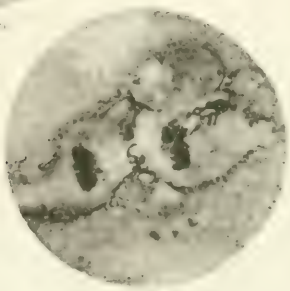


Fig. 7

is most marked in young animals, and in those cases in which no break was made in the tissue by the application of the caustic. These changes in some cases begin twelve hours after the injury, and twenty-four hours afterward there are numerous nuclear figures in the tissue. The first change seen in the corpuscles preceding division is in the protoplasm. In staining the normal cornea with the ordinary nuclear stains, only the nucleus is colored and that slightly. In the regenerating cells the protoplasm becomes more abundant, slightly granular, and the whole mass stains. The nucleus changes its character. It becomes round or oval, more granular, and stains more deeply. The ordinary process of nuclear division then takes place. While this is going on the protoplasm increases still more in amount, and long protoplasmic branches are given off which extend up into the necrotic area. All the processes of the cells extend in this direction only. No processes are given off in the opposite direction. At first the protoplasmic branches are devoid of nuclei, afterward the young nuclei make their way into the branches and active nuclear division takes place in them.

The cell growth is not homogeneous, affecting all parts of the circle, but seems to be especially marked in certain places in groups of corpuscles. In these places the ground substance is reduced to very small amounts, the whole area being taken up by the growing cells. In general the growing branches are long and pointed. In places they become broader, the protoplasm increases, processes are given off, and a new typical corpuscle is formed in the course of such a branch. The length of some of the processes is remarkable. I have frequently seen them so long that they pass beyond the field of a 1 mm. objective. They always extend in the same plane and between the fibers; none seem to penetrate the over and underlying planes. Four days after cauterization with caustic potash the central eschar is filled

with these branches and with new corpuscles formed from them.

In these growing cells a great variety of forms of cell inclusions will be found. Most of the included cells are of leucocytic origin, though the necrotic corneal corpuscles form some part of them. They are found both in the main body of the growing cells and in the processes. Most of them are not in close contact with the protoplasm, but are surrounded by a clear space which probably represents a digestive vacuole. Unchanged leucocytes, with the silver outline around them, may be found alongside of the cells, and every transition between these cells and mere fragments of protoplasm may be seen. The first change in the included cells is in the nucleus, which becomes separated into fragments. These may be retained in the cell, or fragmentation of the protoplasm may take place at the same time, often a small portion of protoplasm being left around the nuclear fragments, and these may be included in different parts of the growing cell. The cell inclusions formed in this way are of special interest in view of the importance which has been assigned to these particles when they are found in the growing cells of tumors. It seems perfectly evident that the leucocytes serve here as food for the growing cells; that they are not necessary is shown by the fact that equally active processes of regeneration are found in cases in which there are no leucocytes. The regenerative processes are usually limited to the row of corneal corpuscles immediately adjoining the necrotic area. Only occasionally are regenerative changes found in the corpuscles farther towards the periphery.

We have already alluded to the partial and complete fragmentation of the granular leucocytes when passing through the tissue. These fragments are also taken up by the corneal corpuscles in their vicinity. Most frequently they lie close to the nucleus, which may be deeply indented, and in sections made across the indentation

they seem to be completely enclosed in the nucleus. Each fragment is surrounded by a clear space in the protoplasm. They frequently contain the brightly stained eosin granules of the cells from which they are derived. They may also be found in the non-granular leucocytes, and in these the brightly stained masses of eosin granules make a sharp contrast with the non-granular protoplasm. They do not seem ever to be included in cells of the same character as those from which they are derived.

A new formation of blood-vessels in the cornea is always seen when the central inflammation is intense, or when a large area of necrosis has been produced. It seems to be intimately connected with the processes of regeneration, though when the area of necrosis is small, complete regeneration may take place without any vascularity. It is most pronounced in the intense inflammations produced by aureus inoculation. The new formation of blood-vessels takes place around the entire circumference of the cornea in case the inflammation is exactly central, or from the nearest point of the margin in case the inflammation is not central. The growth of vessels seems to be more active in the region of the insertion of the ocular muscles than elsewhere. The first evidence of new formation of vessels is seen forty-eight hours after injury, in an active proliferation of the cells of the large veins, from which the emigration has taken place. The tissue here is filled with leucocytes and lymphoid cells, and, among these, large protoplasmic outgrowths from the vascular cells appear.

It has been impossible, in my specimens, to follow the exact details of the beginning formation. A short while later, masses of cells, always preceded by a pointed cell, grow up into the corneal tissue. Red blood corpuscles appear between and around these cells, and finally a space is seen among them which is filled with red corpuscles and leucocytes. This mode of formation corresponds with that ordinarily described. In other cases

the process seems different. Large numbers of red corpuscles appear in the cell spaces immediately around the vessels, and these seem to become surrounded by the growing cells, and in this way converted into vessels. In one specimen it was possible to show a growing vessel opening into a cell space which was filled with red blood corpuscles and which extended from this for a short distance between the fibers. The corneal corpuscles do not appear to take any part in this new formation of vessels. They remain unchanged in the vicinity of the growing vessels. The vessels supplying the conjunctiva show no changes. The new vessels are formed exclusively from the plexus of veins around the edge, which should be regarded as the essential vessels of the cornea.

It is not the purpose of this paper to describe the abscess formation and ulceration produced in the cornea by inoculation with the S. P. Aureus. My purpose has been mainly to show the different sorts of leucocytes which enter the tissue and the part they severally play in the inflammatory process. What we have seen take place in the cornea is applicable to the various forms of inflammation which may be produced in other tissues of the rabbit. In studying inflammatory processes in man it has not been possible for me to separate so clearly the different forms of leucocytes from one another, for the distinctions do not appear to be so marked in man as they are in the rabbit. We are dependent entirely on chance for our material, and the conditions of the inflammation are to a great extent unknown. Anyone who has studied the character of the cells in the exudation in a number of cases of acute croupous pneumonia must have been struck with the great differences in the character of the cells in the alveoli. A comparative study of these cells and the condition under which they appear is being undertaken in the pathological laboratory of the Harvard Medical School.

December 28, 1898.

DESCRIPTION OF PLATES.

Plate I.

Fig. 1.—Section of cornea stained with nitrate of silver, showing a nerve and cell spaces in the tissue. 16 mm. obj., 4 comp. ocular.

Fig. 2.—Section of slightly œdematous cornea, showing silver lines between corneal fibers. 16 mm. obj., 4 proj. ocular.

Plate II.

Fig. 1.—Section of normal cornea, showing cell spaces with granular leucocyte between the fibers. Observe in the leucocyte the filamentous thread of nuclear substance between the larger portions of nucleus. Nitrate of silver and hematoxylin. 8 mm. obj., 4 proj. oc.

Fig. 2.—Section of normal cornea showing granular leucocyte in cell space. Nitrate of silver and hematoxylin. 8 mm. obj., 4 proj. ocular.

Fig. 3.—Section of cornea 48 hours after central inflammation induced by nitrate of silver, showing leucocytic infiltration between the fibers. Nitrate of silver and hematoxylin. 16 mm. obj., 4 proj. ocular.

Plate III.

Fig. 1.—Flat section of center of cornea 18 hours after inoculation with staphylococcus aureus. The corneal corpuscles are destroyed, and there is infiltration with granular leucocytes in cell spaces and between fibers, Nitrate of silver and hematoxylin. 8 mm. obj., 4 comp. ocular.

Figs. 2, 3, 4, 5, 6, 7.—Section of cornea 24 hours after staphylococcus inoculation, showing granular leucocytes in tissue. At the lower end of the leucocyte shown in Fig. 4 a small portion of the protoplasm is being thrown off. Observe particularly the outlines of the cells. Stained in phosphotungstate hematoxylin. 2, 5, 6, 7, 2 mm., obj., 8 comp. ocular. 3 and 4 same obj., 4 comp. ocular.

Fig. 8.—Granular leucocytes in tissue. Eosin and methylene blue. The granules in the cells are so fine as to be nearly invisible. Compare the granules here with the granules in the other cells stained with phosphotungstate hematoxylin. 2 mm. obj., 4 proj. ocular.

Fig. 9.—Non-granular leucocytes in cell space with corneal corpuscle. Observe in these the absence of the ,sharply stained cell membrane. Phosphotungstate hematoxylin. 2 mm. obj., 4 proj. ocular.

Plate IV.

Fig. 1.—Corneal corpuscle with fragments of granular leucocytes adjoining nucleus. There is also a non-granular leucocyte, probably in same cell space. Phosphotungstate hematoxylin. 2 mm. obj., 4 comp. ocular.

Figs 2, 3, 4.—Degenerative fragmentation of corneal corpuscle with direct division of nucleus. 2 mm. obj., 8 comp. ocular.

Fig. 5.—Group of proliferating corneal corpuscles adjoining central lesion. Nitrate of silver and hematoxylin. 4 mm. obj., 4 proj. ocular.

Figs. 6 and 7.—Nuclear division in corneal corpuscle adjoining central lesion. Nitrate of silver and hematoxylin. 2 mm. obj., 4 proj. ocular.

Fig. 8.—Formation of blood-vessel. A cell space filled with red blood corpuscles which have penetrated between the fibers beyond this. In the lower portion this space communicates directly with a blood-vessel. The growing endothelium of this is advancing over the space. 2 mm. obj., 4 proj. ocular.

IRIDOCYCLITIS WITH LENTICULAR CATARACT: TRUE GLIOMA OF THE EYE; PERITHELIOMA OF THE EYE; PIGMENTED PERITHELIOMA OF THE EYE.

JOHN M. BEFFEL.

Case 1. Iridocyclitis With Lenticular Cataract.—From the practice of Dr. Ritter. Case first seen in June, 1898. A girl of 10 years of age, with inflammation of the left eye for one week, and traumatism two years previous from finger nail. Examination showed conjunctiva injected, pupil dilated irregularly under the atropine, iris adherent, slight opacity below the pupil. Diagnosis of iridocyclitis with cataract. The treatment was enucleation on July 8, 1898. Microscopic examination of the eye showed leucocytic infiltration of the anterior chamber on the posterior corneal wall, also upon the anterior and posterior surfaces of the iris; this infiltration extending to and surrounding the lens and extending laterally over the ciliary processes. The lens shows capsule normal on anterior surface with its anterior epithelium beneath; the posterior capsule normal, lens fibers at the equator and posteriorly having undergone a hyaline degeneration, at the equator large open spaces filled with a clear fluid, presumably the liquor of Morgagni, this degeneration occupying the posterior one-fourth of the lens, extending also to a slight extent anteriorly.

Case 2. Glioma of the Eye.—In the practice of Dr. Ritter. Case was first seen July 29, 1898. Boy 6 years of age, supposed traumatism of eye by table fork; no pain at any time before or after the supposed injury. Examination showed diffuse conjunctival and scleral injections, rough and uneven cornea, eyeball bulging, lens cataractus. Diagnosis of iridocyclitis with cataract.

Treatment was iridectomy September 22; enucleation October 10, 1898. Microscopic examination shows complete detachment of the retina, anterior portion of the retina deeply convoluted; posterior chamber and space between choroid and retina filled with granular amorphous material. The elements of the retina normal except in one place just posterior to the lens. At the point just mentioned we find a tumor about two millimeters in diameter which is developing from the neuroglia fibers about the ganglia of the retina not far from the granular layers which may be seen only slightly disturbed; but having no part in the tumor formation.

Histological Structure of the Tumor.—The periphery of the tumor is composed of irregular fibers; as we go into the tumor the fibers are more irregularly branched, many cells showing eight or ten branches; between these cells are fine fibrils with now and then a small nucleus showing little or no cell protoplasm. Fine capillaries are seen traversing the tumor. There are two small areas of calcareous degeneration. Specimens stained with Mallory's phosphotungstic acid hematoxylin followed by one-half minute in Van Gieson's stain showed characteristic neuroglia or spider cells.

Diagnosis.—The structure of this tumor is similar to that of glioma of the brain and is developing from the Mullerian fibers, therefore I believe this to be a specimen of true glioma of the retina, and is not to be confused with those so-called gliomata supposed to originate in the granular layers of the retina and which many pathologists believe to be small round-cell sarcomata.

Case 3. Perithelioma of Eye.—From the practice of Dr. Starkey. A girl, 2½ years of age, suffered an injury to the nose in a fall, and two weeks later the mother noticed the interior of the eye to look white. A glioma was found upon examination, which almost filled the vitreous chamber; and enucleation was performed. There has been no return after two years. Microscopic exam-

ination of the eye shows a tumor mass between the retina and choroid, which has caused a complete separation of the retina. In one place there is apparently a proliferation of the inner granular layer; the cells appear to be developed in mantels about the blood-vessels, in places the cell masses being fused, there being little or no intercellular substances. This tumor may originate either in the endothelium of the perivascular lymph spaces or from the connective tissue of the blood-vessels. The former origin is believed to be the one in this case. Such a tumor is a sarcoma and also called a perithelioma.

Case 4. Pigmented Perithelioma of Eye.—From the practice of Dr. Gradle. The eye, upon macroscopic examination, is as follows: the cornea normal, three brownish-black spots about 2 mm. in diameter in the sclera, cross-section of the eye reveals the vitreous chamber almost filled with an irregularly black, and grayish tumor mass. Microscopic examination: The retina was entirely destroyed except at the ora serrata, where it blends with the tumor. A continuation of the fibrous layer is reflected toward the lens. The vitreous chamber was almost filled with tumor tissue. The lamina basalis is intact in all parts. The sclera is unmodified except for a thinning at places. Just inside of the lamina basalis is a non-pigmented layer of cells about 50 microns in thickness. In one place this forms a nodular area, 2 mm. in diameter, composed of masses of cells forming solid cylinders about blood-vessels. The whole of the internal tumor mass is made up of similar masses, some degenerated, others containing more or less pigment. The chorio-capillaries are normal, which with the lamina basalis are the only normale structures in the choroid. The tumor masses are composed of blood-vessels surrounded by proliferating cells, probably endothelium from the perivascular lymph spaces.

October 13, 1898.

THE DUCTLESS GLANDS.

REPORT OF A NECROPSY IN A CASE OF ACROMEGALY.

LOUIS J. MITCHELL AND E. R. LE COUNT.

The clinical features of the case about to be reported have been fully described by Church and Hessert (*Medical Record,* May 6, 1893) so it is only necessary to recall a few data.

The patient, A. K., was 41 years of age when he first came under observation in 1893; was 162.5 centimeters in height, and weighed 81.1 kilogrammes. He had apparently been afflicted with the disease for many years, for we learn that while still a young lad, on going to buy a pair of gloves, his hands were found to be unusually large, needing a man's size. Some ten years before this examination he came to this country and began to attract attention on account of his large head and hideous aspect. When first seen, he was under treatment in the County Hospital for syphilis, and left after a stay of some length. Nearly two years later, in January, 1895, he was taken sick, and, after staying in a lodging-house for a week or so, started to walk to the hospital with a friend's assistance, but fell dead at the corner of the hospital grounds. The necropsy, twenty-four hours' post-mortem, showed death to be due to lobar pneumonia; the cranium and bones of the extremities on one side were dissected out and macerated.

Necropsy Report.—The brain appears normal except for an injection of the meningeal vessels. The hy-

pophysis is very much softened, and removed only with considerable difficulty from the fossa, which is much enlarged. It consists of a semifluid mass of grayish-red tissue, which does not seem to be greater in bulk than the normal hypophysis.

The thyroid weighs seventy grammes; the left lobe measures 6.8×3.1×2.5 centimeters; the right, 7.5×4.3×2.5 centimeters. On section it appears normal. No thymus gland or remains of thymus are found.

The right pleural cavity is empty and free from adhesions. The left contains a small amount of sanguinolent serum.

Lungs: The right lung weighs 560 grammes; it measures 25×18.7×10 centimeters. There are many spots of black pigment in the pleura. The lung floats and crepitates throughout; the anterior and lower borders of the lower lobe are emphysematous; there are no changes about the apex. On section, a small nodular area is found in the lower external portion of the upper lobe which contains a cavity 1.5 centimeter in diameter, filled with grayish pus. The surrounding lung tissue is consolidated to a slight extent; the remainder of the lung shows no areas of consolidation, but appears engorged with blood. The left lung weighs 1230 grammes; it measures 26.2×23.6×8.7 centimeters. The pleura over the upper lobe is covered with a soft fibrinous exudate, easily removed. This lobe is massive and firm, and on section shows a gray, granular surface from which casts of the alveoli and small bronchioles are easily scraped; portions of this lobe sink at once when placed in water. A distinctly mucopurulent material escapes from the larger air-passages on pressure. The auricular part of the upper lobe, the anterior margin, and extreme apex consist of much-dilated air sacs, easily collapsed by pressure. The lower lobe contains but little air, much fluid, and some areas of consolidation in its center.

The pericardial cavity contains a small amount of

clear fluid; its surfaces are smooth and of an even color throughout.

Heart: Unopened it weighed 450 grammes. There is a thick deposit of fat over the base of the heart, measuring from five to seven millimeters in thickness. The mitral valve admits two finger tips; the tricuspid, five. The cavity of the left ventricle measures eight centimeters long; its wall, 2.8 centimeters; the cavity of the right ventricle, 8.7 centimeters; the wall, 6 to 9 millimeters. The left ventricle is empty; the right ventricle and auricle contain a small amount of "goose-fat" clots. The endocardium in the left ventricle shows a few yellowish thickenings just below the aortic valves for a distance of one to two centimeters. The chordæ tendinæ are shortened and the muscular papillæ thickened in the left ventricle, some of these latter measuring two centimeters in length. The mitral valve is slightly thickened at its free edge. The tricuspid and pulmonary valves show no changes. The auricles and auricular appendages appear normal, and the foramen ovale is closed. The aortic valves are thickened at their points of contact and attachment. The myocardium is of a firm consistence throughout, of a light-brown color, and shows on close examination minute bluish-white thread-like streaks which run parallel with the muscular fibers and appear located, as a rule, around the blood-vessels.

The coronary orifices are open. Both coronary arteries are very much dilated and tortuous. The right is found with its lumen empty to the apex of the heart. The left measures thirteen millimeters in diameter three centimeters from its opening in the aorta, and contains a few atheromatous plaques in its wall—most numerous near the aorta.

Aorta: Just above the valves are many scalelike plaques, completely calcified, which readily shell out, also other yellowish areas which show no signs of calcification. In the thoracic aorta many similar calcified

plates are met with, as well as grayish and yellowish raised areas. Some of the areas of calcification measure a centimeter across.

The diaphragm extends upward to the fourth rib on the right side and to the fourth interspace on the left side.

The abdominal cavity contains only a slight amount of fluid. The peritoneum is smooth and shiny everywhere. There are no adhesions except a few about the gall-bladder and hepatic flexure of the colon. The omentum covers the intestines only in part, reaching a point opposite the umbilicus.

The stomach weighs two hundred and eighty-five grammes. It measures 26.2×11.2×7.5 centimeters. The pylorus admits one finger easily. The mucosa appears to be thickened, and is covered with considerable grayish-brown mucus. It is thrown into many folds, which generally conform to the rugæ in direction; these folds are almost entirely obliterated by stretching.

In the intestines the solitary follicles and Peyer's patches are found enlarged and considerably bile-stained. Considerable mucus, exceedingly viscid, adheres to the mucous membrane of the small intestine. The mesenteric glands are considerably enlarged and contain pinpoint ecchymoses. The appendix, short and thick (four centimeters long), lies on the right ilio-pectineal line.

Liver: Weight, 3530 grammes. It measures 29.3×20×13.7×11.8×8.7 centimeters. Externally about midway between the superior and inferior borders, it presents a groove extending transversely from the fissure between the right and left lobes to the right border; this constriction marks off about one-fifth of the right lobe. The fissure between the right and left lobes is much exaggerated, being about 6.2 centimeters in depth. The surface of the liver is irregularly nodular, the elevations measuring 0.5 to one centimeter in diameter. Between these elevations are bands of white connective tissue in

the capsule. The surface of the cut section is rough; the islands of liver tissue which project as elevations measure from one to five millimeters across. In consistence it is firmer than normal; in color, a uniform grayish red. The gall-bladder is empty and the bile passages are patent.

Spleen: The weight is 450 grammes, and it measures 18.7×10×5 centimeters. The capsule is wrinkled and the pulp softer than normal; the Malpighian bodies are faintly visible; the connective tissue is not increased. A few small, whitish areas in the capsule occur, at which points the capsule is thickened.

The pancreas weighs 105 grammes and measures 23.7×3.7×1.2 centimeters. On section no changes from the normal are visible.

The adrenals appear normal; the left weighs 20 grammes, the right sixteen grammes. The left measures 7.5×4.3×1.2 centimeters; the right measures 5×4.3×1.2 centimeters.

Kidneys: The left weighs 300 grammes; it measures 15×6.8×5 centimeters. Externally are many depressed areas, 0.5 to a centimeter in diameter and depressed below the surface one to two millimeters. There are also many small subcapsular cysts possessing clear contents, averaging one millimeter across. About thirty of these are found on one side of the kidney. On section the cortex and pyramids appear of the same shade of color, the cortical markings distinct, labyrinth wider than normal, the line between pyramid and cortex indistinct. The cortex measures 1 to 1.5 centimeter; the pyramid, 2 to 3 centimeters. There is an excess of fat in the pelvis, and the capsule is quite adherent. The right kidney weighs 360 grammes and measures 15×8.4×3.7 centimeters. It answers to the same description as the left kidney.

The other organs were negative.

Anatomical Diagnosis.—Lobar pneumonia, fibrinous

pleuritis, cirrhosis of liver, softening of hypophysis, and enlargement of the viscera.

Microscopical Examination.—The hypophysis, as before stated, was so much softened that solid pieces could not be obtained, but a small amount of this semifluid tissue was collected and hardened in alcohol. Sections stained with hematoxylin and eosin show many fields where the tissue is not much torn; such fields are made up more or less of short rows of cells resembling tubules. In certain fields the row formation is more marked than in others; small capillaries run between the rows of cells. The cells forming these rows are more or less columnar, and certain single cells show this better than others; the arrangement in rows is more a dense linear accumulation of cells than an appearance due to the columnar or cubical character of the cells. These cells possess oval or circular nuclei which stain darkly—the nuclear membrane being well differentiated; many of the nuclei are large, many irregular in contour. Both nucleus and cell body vary in size considerably. The cell bodies are quite large; they stain well with eosin, as a rule, but occasional cells have a disposition to take the hematoxylin stain in place of the eosin in the cell bodies. Some large cells occur with the nucleus nearer one edge of the cell. The areas where tubule or row formation does not prevail seem to be made up of similar cells, but much scattered and disarranged. The connective tissue is very scanty and is confined to the region immediately around the blood-vessels. The blood-vessels show no changes; no karyokinetic figures are present. Sections of this hypophysis were submitted to Dr. Adolph Meyer, of Worcester, Massachusetts, who pronounced the condition to be one of hyperplasia.

Lung: The left upper lobe shows the microscopic features ordinarily seen in lobar pneumonia. The alveolar contents are markedly fibrinous, with considerable degeneration of cells—i. e., failure to stain. There is

also considerable blood in the alveoli, and a marked perivascular and peribronchial deposit of coal pigment.

The abscess wall from the right lung shows a fibrous wall beset with vessels; there are no caseation or tubercles in the surrounding tissue. The lining possesses many polymorphonuclear leucocytes.

Heart: The pericardial covering shows a slight increase in thickness of the under layers, with here and there larger bands of fibrous tissue extending into the myocardium. These bands are usually provided with vessels. The endocardium appears unchanged.

There is considerable pigment opposite the poles of the nuclei in the shape of small, golden-brown granules. Both segmentation and fragmentation of heart-muscle fibers occur, the fragmentation being the more marked. The nuclei of the muscle fibers exhibit various sizes ("giantism," "hyperchromatosis"). The arterioles show a slightly thickened tunica media; the connective tissue between the muscle fibers is but little increased. A few foci are seen where the muscle fibers have disappeared, and their places have been taken by a slightly granular grayish tissue in which are scattered spindle-shaped and oblong nuclei.

Stomach: The mucous membrane is very atrophic; the glands are fewer than normal and infiltrated with deeply staining round cells, many of which are fibrillated. There are accumulations of brown granules of pigment at the bottom. At certain points the round cells are accumulated in round foci internal to the muscularis mucosæ, which is thickened. The submucous coat is narrow and consists of a large amount of fibrous tissue devoid of nuclei. The tunica media of the vessels is thickened.

Small Intestine: The mucous membrane is very atrophic; the glands are very short; there is a marked increase in small round cells which stain darkly in the mucous coat. There are also many spindle-shaped cells,

gathered around and between the glands. The muscularis mucosæ is very much thickened, and the connective tissue in the submucous coat is also increased in amount, and is hyaline in character. The vessels show thickening of the tunica media.

A mesenteric lymph gland is found to possess an increase in connective tissue; there is an increase in the number of blood-vessels, as large sinuses which are filled with blood; a marked hyperplasia of the finer gland reticulum, and pigmentation with blood pigment.

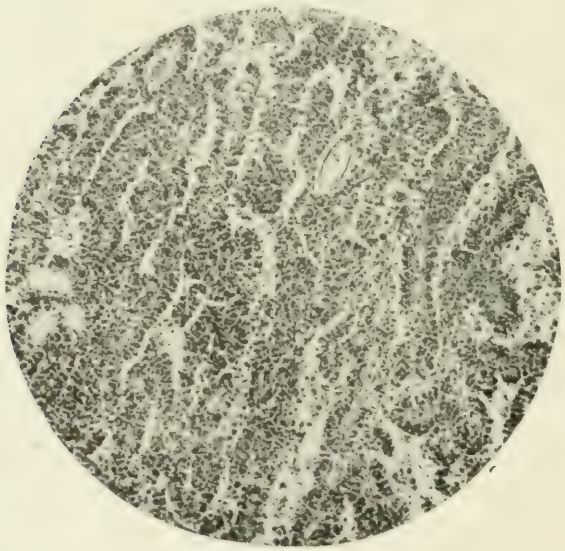


Fig. 1.—Section of hypophysis. × 75.

Liver: The lobular arrangement of the liver cells is much broken up by the connective-tissue increase.

The liver cells show many glycogen holes here and there. There are very few fat holes. The nuclear staining is uniformly good; nuclear vacuolation occurs; dilatation of the capillaries is very marked.

The connective-tissue increase is mainly in the shape of large, coarse bands, and these bands consist of quite

mature connective tissue. There are numerous vessels with thin walls filled with blood in these bands. The intermediate-sized bands of connective tissue are more embryonal, and in these the vessels are more numerous. In addition to these there are minute bands of connective tissue made up mainly of rows of round cells. Increase in bile ducts is not so marked as is usually seen in atrophic cirrhosis.

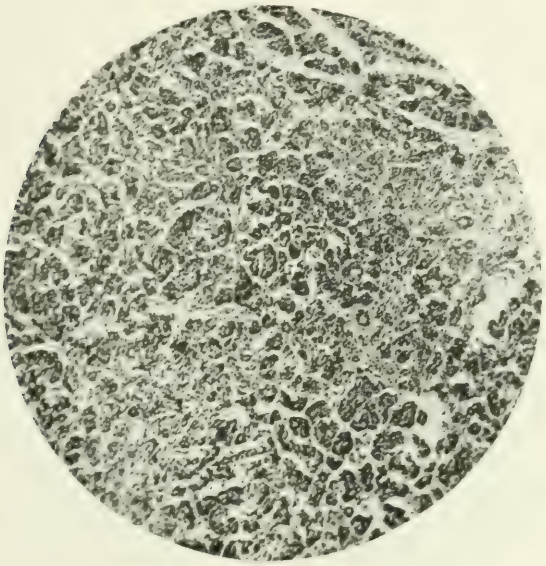


Fig. 2.—Section from pancreas. 75.

Spleen: The Malpighian corpuscles are irregular, not well defined, usually smaller than normal, but otherwise negative. The spleen pulp cells are almost entirely made up of small round cells; nucleated red corpuscles are found in the sinuses; polymorphonuclear leucocytes are very infrequently seen. There are numerous accumulations of blood pigment. The blood-vessels all show great thickening, especially in the tunica media. There are no degenerative or necrotic processes observed. The connective tissue is slightly increased in the finer reticulum;

the large bands are heavy and contain fewer nuclei than normal.

The pancreas exhibits a marked increase of stroma, which is largely hyaline; in this are small arterioles with their middle walls thickened. The connective tissue about the larger ducts is very much increased in amount, and the lining cells are several layers thick. The ducts are irregular and tortuous; some desquamation of the cells occurs. The connective tissue about the acini appears heavier and more easily seen than is usually the case. There are numerous small foci of hemorrhage and dilated veins filled with blood.

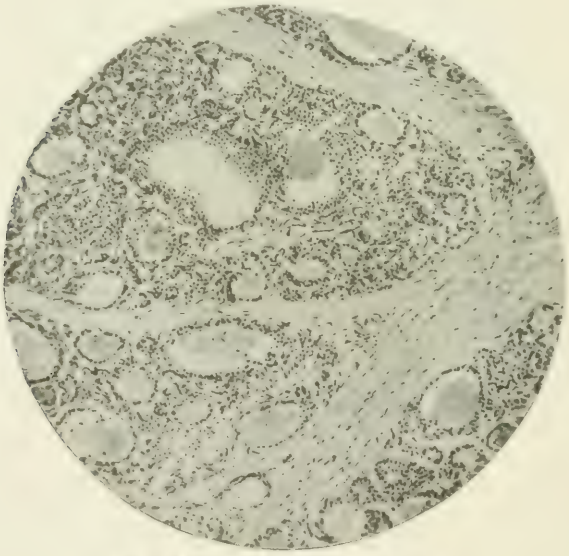


Fig. 3.—Section of thyroid gland. 75.

Adrenals: There is marked pigmentation with blood pigment. The engorged vessels in the medulla contain a marked excess of leucocytes. The nuclear staining is uniformly good. The trabeculæ leading into the gland from the capsule, and also the capsule itself, seem to be heavier than normal.

In the thyreoid there is an increase of both interlobular and interacinous connective tissue, a great diminution in size of the follicles, and thickenings in the tunica media of the blood-vessels.

Kidneys: The glomeruli show usually a slight capsular space; they are filled with blood; there is a marked increase in thickness of the walls of the capillary loops. There are numerous oblong nuclei in the glomerulus; many glomeruli are smaller than normal, in which case Bowman's capsule is usually thickened. There is a connective-tissue increase at the arterial pole of the glomer-

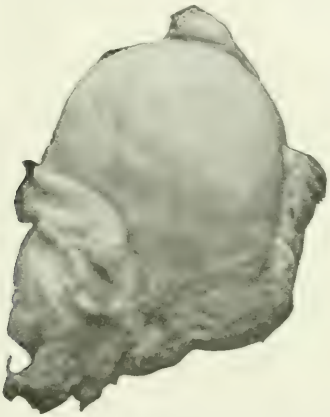


Fig. 4.—Front view of the hypophysis growth. Rathmell's case, actual size.

ulus in the shape of short, spindle-shaped cells. The convoluted tubules show good nuclear staining; the protoplasm is very granular. The collecting tubes are negative. The blood-vessels show a marked capillary engorgement both in the pyramids and cortex. There are similar changes in the small arterioles as were observed in other viscera. The connective tissue of the kidney is not increased. The subcapsular cysts show a lining of short cubical cells. There is a deposit of blood pigment in the pyramids.

Cranium: The antero-posterior diameter is twenty

centimeters; the bitemporal, fifteen centimeters; the greater part of the coronal suture is obliterated outside, and entirely so inside; the same holds good for the sagittal, but the lambdoid is open on both faces. The metopic suture is present for 2.5 centimeters at its lower end.

The ridges for muscular attachments are well marked. This is so much the case over the mastoid and suboccipital regions that the surface is studded with masses and nodules of bone from three to six millimeters in thickness, from which the occipital protuberance stands out as

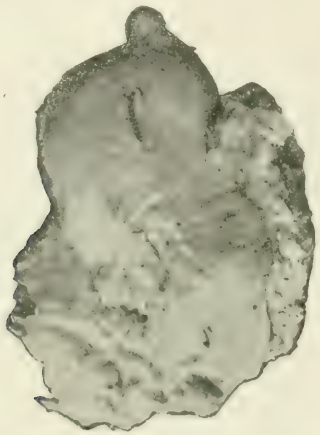


Fig. 5.—Back view of the hypophysis growth, Rathmell's case, actual size.

a large boss ten millimeters long. The external occipital crest is very well marked also, forming a sharp ridge. The styloid process is only twelve millimeters long.

The malar bones are enlarged and very prominent, causing a deep hollow below them. The suture between the malar and maxilla is obliterated on both sides.

The supraorbital ridges are enormous, as may be seen from the photograph. A piece was removed from the anterior wall of the frontal sinus, showing that the bosses are not due to the thickening of the plates of the skull, but to increase in the size of the sinuses.

The orbits were enlarged in both their transverse and vertical diameters. The sphenoidal and sphenomaxillary fissures were enlarged also, the latter being six millimeters wide. The external pterygoid plates are very rough and thick. The hamular process is large—twelve

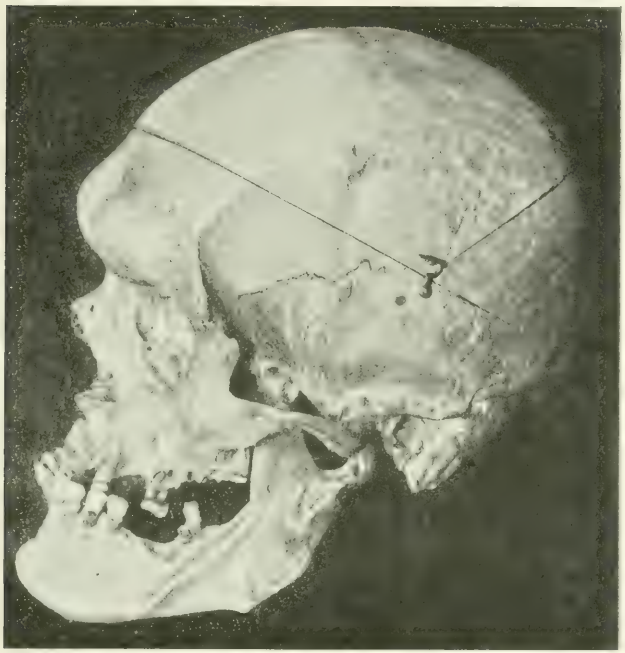


Fig. 6.—View of the skull from outside.

millimeters. The first and second molars are missing on both sides below, and the first and second on the left above.

The nasal septum is deviated to the right. The external auditory meatus is enlarged, but there are no exostoses.

The mandible is asymmetrical, the right ramus being two centimeters longer than the left. This is partly compensated for by the increased length of the left coroid process. The condyles are three centimeters wide;

the left coronoid process is unusually high (three centimeters), thus making the sigmoid notch on that side narrow and deep. The right coronoid process is but twenty-three millimeters high. The muscular ridges are well developed; there is a well-marked osteophyte,

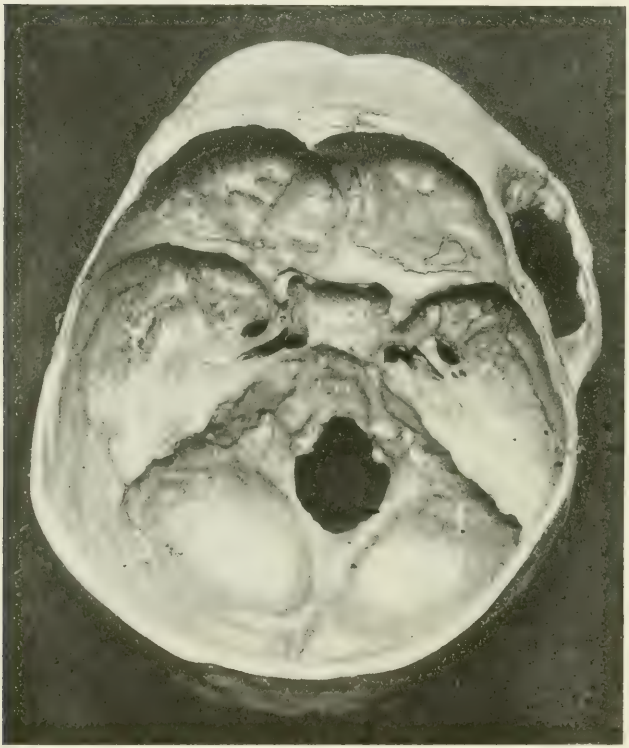


Fig. 7.—View of skull—slightly tilted—from the inside, showing the enlarged sella turcica, also Wormian bones.

eight millimeters thick, at the angle of the jaw on the right side. The bone, as a whole, is very massive and thick, the body much inclined forward. The rami join the body at an obtuse angle, resembling that of the edentulous jaw of old age.

On the interior of the cranium there are numerou

osteophytes over the base and one on the vault measuring 2.5 centimeters by 12 millimeters. There are two Wormian bones in the roof of the right orbit and four in the left. The superior border of the petrosa is unusually sharp on both sides. The sella turcica measures 4.5 $\times$2.5$\times$2 centimeters; the floor is pitted by several large holes. On the right side the boundary between the sella and middle fossa of skull has quite disappeared. On the left it remains in part. The anterior clinoid processes are unusually well marked; the dorsum sellæ is very thin and parchmentlike. The bones of the skull are not thickened; indeed, over the temporal region they are unusually thin.

The clavicle is 15.5 centimeters long; the sternal end is prominent, and the articular surface for the sternum increased in size. The muscular impressions are unusually well developed on this bone as elsewhere.

The scapula is 15.5 centimeters deep. The scapular index is 64.6. The supraspinous and subscapular fossæ are unusually well marked. The muscular impressions on vertebral border, and especially the axillary border, are large and rugose.

In the upper extremity, the humerus is 32.5 centimeters long, the ulna 23 centimeters, the radius 25 centimeters. The muscular impressions in the upper part of the humerus and ulna are again noticeably prominent. The lower end of the radius is very large; the carpal bones are unchanged. The metacarpal bones and phalanges are rough; the distal phalanges very large—widened, thickened, and rough.

In the lower extremity the femur is 42.5 centimeters long, thick, and clumsy looking; the impression for the glutæus maximus is well marked, almost forming a third trochanter; otherwise there is little change. No change is to be found in the tibia or fibula. The insertion of the tendo Achillis into the calcaneum is marked by an irregular mass of osseous tissue. The ungual phalanges.

like those of the upper extremity, are thick, flat, and rough—studded with osteophytes.

There was no kyphosis.

October 11, 1897.

SARCOMA OF THE THYROID GLAND.

PAUL F. MORF.

Although the occurrence of the enlargements of the thyroid body was known for a long time, it was not until within a comparatively recent period that the discovery of malignant tumors having their origin in this gland was made. In 1817 Alibert (quoted by Bircher) reported a case of true sarcoma of the thyroid body. Raynaud, in 1838, under the title of "Thyrosarcomie," gives a report of an encephaloid sarcoma with metastatic foci in the lungs and liver, but he unfortunately gives no description of the microscopic findings. Förster, in 1860, gave an accurate and careful description of one of this class of neoplasms. Virchow mentions the malignant tumors of the thyroid, but gives no data as to their occurrence, and no description of the tumors themselves. He also makes the statement that he saw one sarcoma of the thyroid gland.

The credit of being the first to materially advance our knowledge of the clinical and pathologic manifestations of the struma maligna, and place it on a substantial anatomic basis, belongs to Kaufmann, who, in 1879, very minutely described a series of cases of malignant thyroidal tumors. He collected in all seven cases of sarcoma of the thyroid, three of these having been observed and examined by himself. Since the appearance of Kaufmann's article in 1879, a number of cases have been reported, the majority from the Continent, a few from England, and several in this country. By sifting

the literature on the subject of thyroidal tumors to which I had access, rejecting such cases as might leave any doubt as to the exact nature of the neoplasm, I have been able to collect more or less complete descriptions of thirty-nine sarcomata of the thyroid gland. To these thirty-nine cases I add one more, which I had opportunity to observe while acting as interne in the Cook County Hospital, Chicago. I also add the microscopic description of the tumor of Case 39. The history and clinical findings of this case were reported by Dr. Graham of this city, to whom I am indebted for the material. In his report no details were given in reference to the minute structure of the tumor, mention being only made that the tumor was a round-celled sarcoma. The history of the former of these two cases is as follows:

W. B., American, aged 47, was admitted to the Cook County Hospital, Chicago, Dec. 20, 1897. About one year before admission, he noticed a small swelling in the right side of the neck, near the sternal origin of the right sternomastoid muscle. The swelling slowly increased in size up to about the middle of November, 1897, since when it has grown rapidly; voice unchanged, no dysphagia, occasionally has dyspnea; has lost eight to ten pounds in weight during the last two or three months; appetite good; digestive and urinary systems normal. Previous history: Eighteen years ago patient received an injury in a railroad accident, both clavicles, the left scapula and three ribs being broken; has had gonorrhea twice, but no other diseases; father and mother living and healthy; no one in family had goiter or malignant growth of any kind.

Examination at the time of admission showed the following: Patient is well nourished, adipose tissue abundant, no anemia or cachexia; chest, abdomen and extremities negative. On the right side of the neck, occupying a position corresponding to the location of the right lobe of the thyroid gland, is a tumor about as large as a goose-egg, firm in consistency, no fluctuation; no adhesions to the surrounding structures, or to the overlying skin, which is normal in appearance. On aspiration with an exploring syringe a small amount of blood is obtained. The cervical lymphatic glands are not enlarged, nor involved in the growth. The right sternomastoid muscle and the large vessels on the right side of the neck are displaced to the right and backward. The left lobe of the thyroid gland shows no enlargement.

On Dec. 22, 1897, under general anesthesia, the tumor was

removed by Drs. Moorehead and Brown. The patient made a rapid recovery, leaving the hospital on Dec. 31, 1897.

The tumor removed is about the size and shape of a goose-egg (9x7x6 cm.), firm in consistency, and shows no areas of softening. It is surrounded by a firm connective tissue capsule, which is not perforated or broken through at any point. On section the cut surface is slightly moist and glistening, having a dark red color in some places; elsewhere it is grayish and yellowish in color.

Sections taken from the part where the tumor tissue bordered on the glandular tissue, hardened in formalin and alcohol, stained with hematoxylin and eosin and mounted in Canada balsam, present an interesting picture.

The tumor tissue proper is made up of round cells of intermediate size, and of spindle cells. They are closely packed together and almost no intercellular substance can be made out. The protoplasm of the tumor cells is very scant in many places. The nuclei are large, some oval, some round and others more or less crescentic in shape. The majority take the stain very well, showing a deep blue color; in many, one distinct nucleolus, in many others, two nucleoli can be seen. Some have a deeply stained nuclear wall, while the interior of the nucleus itself is more or less homogenous in appearance, showing no chromatin threads or granules, and staining less intensely than the limiting membrane. In other nuclei the chromatin granules and threads are distinct and scattered irregularly through the nucleus. Some mitotic figures can be found; indeed, they are not rare. In some instances the nuclei show the chromosomes arranged into groups of three, indicating an atypic division of the nucleus. The blood vessels, or more properly the blood-spaces, are fairly numerous. Their walls are formed by the tumor cells, the protoplasm of which stands out sharply against the lumen of the space and is somewhat flattened and drawn out.

Where the tumor tissue borders on the preformed thyroidal tissue, the alveoli of the gland have been changed by compression from their normal round or ovoidal shape, to an irregularly quadrilateral or rhomboidal shape (on section), or appear as spindle-shaped slits. The normal epithelial lining has almost entirely disappeared, as well as a large part of the colloid material, which in the normal gland, or in the colloid goiter, fills the vesicles. The vesicles are either empty, or what is much more common, more or less completely filled by extravasated blood-cells. These for the most part are well preserved, the red showing, in many cases, only the alteration in shape resulting from mutual compression. Some few with disintegrated and pigment granules, having a golden brown color, are found both free and enclosed in cells.

Where the tumor merges into the altered gland tissue just

described, the tumor cells are less closely packed together, gradually becoming more and more scattered and separated by the gland tissue. At the outermost margin of the tumor, sarcoma cells are found lying here and there; 1, in the connective-tissue walls of the altered vesicles; 2, an isolated cell here and there, lying among the extravasated intra-alveolar red blood-corpuscles; 3, an occasional deeply-stained round of spindle-shaped sarcoma cell may be seen lying separate from the neighboring part of the tumor and surrounded by the small amount of colloid material which still remains. Among the tumor cells, small hemorrhagic foci are occasionally seen.

Diagnosis: Primary mixed-celled sarcoma of the thyroid gland.

On April 19, 1898, the patient returned to the hospital. There has been a recurrence of the growth, and he also complains of dysphagia and dyspnea, stating that three weeks ago he received an injury at the inner end of the right clavicle and soon after a small lump appeared there, which has rapidly increased in size. At this time there was found a uniform enlargement at the front of the neck, having a more or less hemispheric shape, the convexity anteriorly, extending from the level of the hyoid bone above to the upper extremity of the sternum below. At the right sternoclavicular articulation there was a tumor, about the size of a walnut, or a little larger, soft and fluctuating, the overlying skin having a deep reddish-blue color and appearing about to rupture. On this account this nodule was removed under local anesthesia. The central mass of this nodule had become softened and consisted of a semifluid mass. The cortical portion was firmer and of a grayish-red color. Very thin sections were hardened in formalin solution immediately after removal of the nodule. Microscopically, the sections showed the presence of numerous round cells of medium size and a few spindle cells. Many mitotic figures were found, sometimes as many as three or four dividing nuclei in a field (1/12 oil-im. ocular iv. Reichert) corresponding with the very rapid growth of the nodule.

Healing of the wound made for removal of this nodule occurred *per primam*, patient leaving hospital again on April 30, 1898. Five days later he was again readmitted. He complained of increased dyspnea, which brought on the exitus four days later.

At the autopsy, April 14, 1898, examination of body, made by myself, gave the following findings: The body is that of a well nourished man, short and heavy set; rigor mortis well marked; lividity in dependent parts; linear scar in the middle of the neck anteriorly about 12 cm. long; a second scar about 8 cm. long over the inner end of right clavicle; general nutrition good, fatty layer moderately thick; no anemia or cachexia.

The pericardial sac contained about 60 c.c. of a slightly

blood-stained fluid; the pericardium is smooth and glossy; there were a few old adhesions over the anterior and posterior surfaces of the right ventricle; left ventricle contained a small amount of dark fluid blood, the right ventricle a small white non-adherent blood-clot. The mitral orifice admitted four finger tips; there were a few yellowish plaques at the base of the anterior mitral cusp; aortic semilunar valves were normal; tricuspid orifice admitted five finger tips, loosely; the valve itself was normal; myocardium is of a brownish red color, with here and there small pale yellowish spots; near the beginning of the aorta were numerous small rounded or irregularly shaped, slightly-elevated yellowish spots 2 to 3 mm. in diameter.

The pleural cavities were empty; the pleuræ smooth and glossy, with a few old adhesions over the right upper lobe. The lungs were dark red in color, floated and crepitated. Near the anterior margins there were small areas of grayish distended air-vesicles; and in the lower part of the left upper lobe was a tumor about the size of an orange, moderately firm in consistence, and on section a dark grayish-red color. A similar tumor having about the same size was found in the lower portion of the right middle lobe, and a third in the lower part of the left lower lobe. In the lower portion of the right lower lobe was a fourth mass about the size of a walnut. These tumors had grown from the lobes in which they were originally situated, and passed across the adjacent interlobar fissure, and into the adjoining lobe; numerous smaller nodules about the size of a pea or hazelnut were scattered through both lungs.

The peritoneum was smooth and glossy, its cavity empty.

The spleen weighed 350 grams: peritoneal surface was normal, but the organ cut with slightly increased resistance. On section, hemorrhagic foci about the size of a pinhead were found.

The liver weighed 2300 grams; surface was smooth, superficial veins congested and cut with normal resistance. On the cut surface the lobular markings were indistinct; in places the periphery of some of the lobules was distinctly yellow. The gall-bladder contained a small amount of dark greenish bile, passages patent.

The kidneys together weighed 450 grams; surface was smooth and even; the stellate veins were somewhat injected. On the convex margin of the right kidney was a small cyst the size of a pea, containing a clear fluid; on section, cortical markings were indistinct; cortex to medulla as 1 to 4; capsule stripped readily, leaving a smooth surface.

The pancreas, stomach, intestines and bladder showed no essential changes. The mesenteric glands were not enlarged.

The scalp, skull, dura mater and brain showed no essential change. Tongue and pharynx were normal. There was calcification of the cricoid cartilage.

On the anterior surface of the neck was an enormous tumor mass, irregularly hemispheric in shape, limited above by the hyoid bone extending downward over the sternum to the point of junction of the first and second pieces of the sternum. The lateral boundaries corresponded to a line drawn from the angle of the inferior maxilla to the middle of the clavicle on each side. The skin over the tumor was normal in appearance, except near the median line, where it was somewhat thinned and adherent to the underlying tumor—site of scar of first operation. Dissecting back the skin showed the two sternomastoid and also the sternohyoid and sternothyroid muscles pressed away from the median line, their fibers pressed apart, and the muscles themselves thin and atrophic. The carotid arteries and the internal jugular vein on each side were displaced outward and backward, were adherent to the tumor mass, but their lumen was patent througout, and their walls had not been perforated at any part by the new growth.

The trachea was compressed from in front and the right, diagonally toward the left and behind, giving the cartilages a more or less oval contour: the lumen of the trachea was not completely occluded at any point. The compression extended downward from a point 1 cm. below the cricoid cartilage, a distance of 5 cm. The trachea contained some bloody mucus.

The esophagus was almost surrounded, near its upper extremity, by a process of the tumor, somewhat cylindric in shape about 4 to 5 cm. long and about 3 cm. in diameter, which passed between the posterior wall of the pharynx, esophagus and the spinal column on a level with the cricoid cartilage.

The main tumor mass was about the size of a child's head, somewhat elastic in consistency throughout the greater part.

In the lower right quadrant, and near the upper left quadrant there were two areas of fluctuation. Section through these fluctuating areas showed in each case a cavity about 5 cm. in diameter, containing a semifluid dark-red mass, the wall of each cavity consisting of tumor tissue.

Elsewhere on section, the cut surface presented a dark-red blood stained appearance, mottled with small yellow points.

Anatomic diagnosis: 1. Recurrent sarcoma of the thyroid gland with metastases in the lungs. 2. Old pleuritis. 3. Emphysema of lungs. 4. Beginning atheroma of aorta. 5. Fatty infiltration of the liver.

Description of microscopic findings of tumor in Case 39: The tumor is composed chiefly of round cells of medium size, their diameter being about equal to twice that of a red blood-corpuscle. There are, in addition, a few small spindle shaped cells. The protoplasm is present in relatively small amount and is homogeneous in appearance. The nuclei are distinct, well stained, and for the most part circular in outline; some few have an oval shape. They have a distinct wall, which

stands out prominently against more lightly stained background of protoplasm. The chromatin is more or less irregularly scattered throughout the nuclei; here and there a nucleus containing two nucleoli, or a cell with a mitotic figure is seen.

Between the cells a small amount of slightly fibrous intercellular substance can be made out. The blood-vessels and blood-spaces are moderately abundant; their walls are formed by long spindle-shaped tumor cells. In some parts of the tumor, small areas are found where there has been a disintegration of the embryonic cells, leaving a granular mass in which no organic elements may be distinguished. Where the tumor tissue merges into the glandular can be seen large spaces filled with disintegrating blood-cells. Some alveoli retain their epithelial lining, but instead of cubic cells are found flattened cells; in other alveoli the alveolar epithelial lining has entirely disappeared, the vesicle, however, containing a small amount of colloid material and an occasional tumor-cell.

Regarding the occurrence of sarcoma in the thyroid gland, the following statements may be made: 1. It is a rare disease. 2. It is more common in those countries where goiter is an endemic disease than in those countries where sporadic cases are the rule. 3. It is more common in persons whose thyroid is the seat of ordinary goiter. 4. It is more frequent in the male than in the female. 5. It occurs oftener in late than in early life.

That it is a rare form of disease hardly needs to be demonstrated. The small number of cases reported points this out as an undoubted fact, there being forty cases in as many years. However, it is perhaps not as rare as would appear from this, for naturally, not all cases are reported, some of which are reported are not accessible, and others not available, because of incomplete or unreliable descriptions. Among 7461 autopsies at the Berne Pathological Institute (Limacher) "struma sarcomatosa" was found forty-four times. In studying the frequency of occurrence of sarcoma of the thyroid, we naturally compare with it the frequency of occurrence of carcinoma of the same gland. While collecting the cases from the literature I was impressed by the relatively large number of reports of cases of cancerous goiter. Ewald, in Nothnagel's "Spec. Path. u. Therap.,"

gives the relative frequency of carcinoma to sarcoma of the thyroid as 3 or 4 is to 1. Kaufmann, in his original paper, reported seven cases of sarcoma and twenty-three of carcinoma of this gland. In considering the subject of the frequency of the occurrence of sarcomata of the thyroid, we include only those cases in which the growth was primary in this gland. Regarding the frequency of secondary sarcomata of the thyroid, the figures of Mueller (quoted by Lücke and Zahn) are in point. Among 102 cases of sarcoma occurring in various parts of the body, 3.1 per cent. produced metastases in the thyroid gland and pancreas. From this it is evident that secondary sarcoma of the thyroid must also be considered infrequent. Of interest in this connection is a communication by Pinner, who reports a case in which a primary sarcoma of the pancreas had given rise to a secondary growth of the same nature in the thyroid gland.

That sarcoma of the thyroid is more common in goiter countries than elsewhere appears to be the case from the following: The largest number of cases have been reported from goiter countries. The figures of Limacher here are also in point, as Berne is one of the acknowledged foci of the ordinary goiter, and while there are no figures on this point that I know of, taken from post-mortems made in this country, still I think it will be generally admitted that no pathologist has found as large a number of sarcomata in this country, where the ordinary goiter occurs sporadically, in an equal number of post-mortem examinations. Just as occasional cases of benign goiter are found in this country, so also scattered cases of the sarcomatous degeneration of the gland are reported in the medical literature of this country. Unfortunately, several of these cases are so incompletely described that they could not be included in the table with the other cases.

The third assertion seems borne out by the following:

Of the appended forty cases, twenty-two gave a history of previous goiter. If we remember how easily a small enlargement of the thyroid is overlooked in a locality where from one-half to two-thirds of the inhabitants are afflicted with the disease (Bircher), and also remember that in many of the histories of the cases reported, no definite statement is made in regard to previous goiter, it is probable that the proportion of cases in which a benign enlargement preceded the malignant growth is larger than appears from these figures. However, a benign enlargement is not a necessary precursor of the sarcoma. In some of the reported cases, the definite statement is made that no previous enlargement was present. As appears from the appended table, no previous goiter was present in eleven cases, or 27.5 per cent. One can therefore scarcely agree with the statement of Braun that "struma maligna" rarely occurs except in cases in which the thyroid is already the seat of goiter. However, statistics based on such a small number of cases are necessarily uncertain, and additional observations are desirable to settle this point definitely.

The influence of sex is shown to be of some importance. Eighteen of the forty cases collected were females, the remainder males. This is contrary to what might be expected from the preponderance of the non-malignant goiter among women.

That sarcoma of the thyroid occurs more frequently in advanced than in early life is a point on which almost all observers agree. One exception to this is Lücke, who says this form of neoplasm is found oftener in young strong persons, although he admits it has been observed at a more advanced age. Separated into decades, the forty cases herewith show the following distribution:

AGES	CASES
20-30	1
30-40	2
40-50	10
50-60	18
60-70	9

TABULAR ANALYSIS OF FORTY CASES OF SARCOMA OF THE THYROID GLAND.

No.	Reported by	Sex and age.	Previous goiter.	Origin.	Microscopic variety.	Cervical glands.	Metastases.	Points of special interest.
1	Förster	F. 60.	. . . . .	Right lobe.	Spindle & stellate cell, bony tissue.	No enlargement.	. . . . .	Adhesions to larynx firm; perforation of trachea.
2	Scheiber	M. 40.	Tumor of neck years before.	Right side.	Alveolar sarcoma; stellate cells.	Involved.	In cranial bones.	Trachea compressed; common carotid, internal jugular and vagus involved in growth.
3	Doléris	M. 55.	Tumor of neck 14 yrs before.	Left lobe.	Fibrosarcoma.	Involved.	. . . . .	
4	Kaufmann	M. 66.	Present for a long time, previously.	. . . .	Spindle-celled sarcoma.	Involved.	In pleura.	Left jugular, innominate and thyroid vein filled by thrombus; thrombus reaches to opening of innominate into cava.
5	Ibid	F. 53.	Since youth.	. . .	Spindle-celled sarcoma.	. .	Anterior mediastinum, both lungs and liver.	
6	Ibid	F. 46.	Three years before.	Left lobe (?)	Struma cystosarcomata.	. . .	. . . . .	
7	Ibid	M. 56.	Long time previously.	Left side.	Small round-celled sarcoma.	. . . .	Mediastinal lymphatic glands.	Compression of esophagus.
8	Ibid	F. 61.	No previous goiter.	Left lobe.	Round-celled sarcoma.	. .	No metastases.	
9	Ibid	M. 53.	. . . . .	. . . .	Spindle-celled sarcoma	. .	In bones, muscles, skin.	Duration approximately five months.
10	Ibid	F. 57.	No previous goiter.	Right lobe.	Round and spindle cells.	. . . .	No metastases.	
11	Neumann	F. 54	Present for 5 years.	. . .	Alveolar sarcoma containing colloid masses.	. . .	Met. alveolar sarcoma in humerus.	
12	Braun	F. 59.	For 20 years previously.	Left lobe.	Lymphosarcoma.	Right side; moderately enlarged.	. . . . .	Duration of disease about four months; compression of larynx and trachea.
13	Heath	F. 55.	. . . . .	Mainly on the right side.	Spindle and round cells and intermediary forms.	. . .	In pleura and lung	Duration about six months; whole larynx displaced; perforation of larynx and trachea below vocal cord by tumor; platysma, sternomastoid, omohyoid and thyroid stretched over growth, thinned and atrophied.
14	Tilleaux	M. 33.	None.	. . .	Fibrosarcoma.	Not enlarged.	. . . . .	Patient presented clinical symptoms and signs of Basedow's disease.
15	Mathieu	F. 69.	None.	. . . .	Round-celled sarcoma.	Involved.	. . . . .	Encephaloid degeneration; trachea surrounded, but not compressed; complete obliteration of middle portion of jugular; right pneumogastric enters the mass and its fibers separated by tumor cells.
16	Bircher	M. 50.	None.	. .	Round-celled sarcoma.	Enlarged.	In lungs.	Adhesions to trachea; duration of disease about six months; cause of death edema of glottis.
17	Schumziger	M. 49.	Tumor of neck many years.	R. side neck.	Round and spindle-celled sarcoma.	. . . .	. . . . .	Foci of softening, cavity formation and calcification; trachea surrounded on three sides; perforated r. side.
18	Braun	M. 59.	Goiter since early youth.	Right lobe.	Round and spindle-celled sarcoma.	Hard and infiltrated	L. vent., 5th costal cart., perichond., pleura, left lung and liver.	Larynx and trachea pressed to the left side; larynx compressed and its cartilage softened.
19	Ibid	F. 46.	Tumor of neck since age of 17.	. .	Cavernous sarcoma.	Enlarged.	In lungs.	Perforation of trachea by tumor; extensive thrombosis of cervical vessels.
20	Ibid	F. 44.	Goiter present for ten years previously.	. . . .	Spindle-celled sarcoma.	Not enlarged.	. . . .	Adhesions to trachea and esophagus; operation, suppuration, followed by erosion of blood-vessel by the suppurative process, causing fatal hemorrhage.
21	Ibid	M. 58.	Tumor of neck 24 years.	Right side.	Vascular round-celled sarcoma.	Enlarged; some hard, some soft.	R lung and in 7th cervical vertebra.	Thrombosis of small veins, coming from the tumor, with tumor tissue.
22	Wölfler	M. 38.	Tumor of neck for 15 years.	Right side.	Fibrosarcoma.	Involved.	. . . . .	Trachea compressed; large blood-vessels of neck (right side) imbedded in tumor mass and pressed outward; duration about ten weeks.
23	Ibid	M. 51.	Tumor of neck 19 years.	Right side.	Angio-cavernous sarcoma.	Infiltrated.	Lungs, mediastinal lymph gland and in left ileum.	Larynx and trachea dislocated toward left; thrombosis of veins of neck; cause of death, pulmonary edema.
24	Ibid	M. 63.	None.	Right side.	Round-celled sarcoma.	. .	. . . . .	Trachea dislocated toward right; duration about four months.
25	Ibid	F. 51.	. . . . .	Left side.	Giant, round and spindle cells.	. . . . .	In dura mater.	Trachea pressed toward right; cricothyroid membrane perforated by tumor; l. sternomastoid muscle infiltrated; jugular vein perforated, thrombosed, thrombus extending upward into sigmoid sinus, downward into r. auricle; thrombus consists of tumor tissue.
26	Ibid	F. 35.	. . . . .	. .	Alveolar angiosarcoma.	. . . .	. . . .	
27	Kobler	M. 62	None.	Right side.	Spindle-celled sarcoma.	Enlarged, cheesy degeneration	Liver, upper part of ileum and in right kidney.	Trachea adherent just below larynx; esophagus compressed, tumor tissue replacing its muscular coat; multiple hemorrhages in brain.
28	Pitt	M. 65	No history of previous goiter.	Left side.	Round-celled sarcoma.	Adjacent glands involved.	. . . .	Growth extends into left jugular, where a clot mixed with growth was adherent; "r. side of heart contained extensive ante- and post-mortem clot, extending into pulmonary artery and showing localized patches of white growth, doubtless carried from internal jugular vein"; duration of disease about four weeks.
29	Shattuck	M. 42.	. . . .	Right lobe.	Spindle-celled sarcoma.	. .	. . . .	Invasion of esophagus and sheath of carotid by tumor.
30	Turner	F. 66	None.	. .	Round-celled sarcoma.	Not infiltrated.	. . . .	Right sternomastoid muscle infiltrated by tumor; infiltration of adjacent fatty tissues; tumor and skin adherent to one another; duration about nine months.
31	Bryant	M. 56.	None.	. .	Round-celled sarcoma.	. .	. . . .	
32	Pick	F. 51.	Tumor for many years.	Left side.	Spindle-celled sarcoma with bony tissue.	Enlarged and infiltrated	Lungs, heart, liver, stomach, intestine, pancreas, dura mater, palate.	Larynx pressed toward r. side; trachea compressed and adherent to the tumor; large blood-vessels and nerve dislocated; esophagus compressed and bent; duration of disease about one year.
33	Ibid	M. 66.	None.	Right lobe.	. . .	Enlarged; infiltrated	. . . .	
34	Lentz	F. 56	Goiter at age of 15.	L. side neck	Chondrosarcoma spindle cells.	. .	. .	
35	Gatti	M. 40.	Goiter since childhood.	Right lobe.	"Sarcoma a cellules polymorphi." Giant, large and med.-sized cells.	. . .	In the lungs.	Trachea and large blood-vessels surrounded by growth; suppuration and abscess formation in tumor; streptococci in blood; duration of disease about 7 months.
36	Stewart	F. 41.	Lump at neck 5 years before	Right side.	. . . .	. . .	. . . .	Larynx displaced toward left side; tumor adherent to lower part of thyroid cartilage and carotid sheath.
37	Limacher	F. 59	Goiter for many years	Right lobe.	Alveolar sarcoma.	Enlarged; hard.	In lungs, manub. sterni.	Tumor had its origin from the endothelium of the blood-vessels; duration about eight months.
38	Ibid	M. 48 5	For many yrs. previously.	. . .	Alveolar angiosarcoma.	. . .	. . .	
39	Graham	M. 60.	Goiter of two years' standing.	. .	Round-celled sarcoma.	. . .	. . . .	Larynx and trachea crowded to r. side; fatty degen. of tracheal rings; when turned flatwise two walls fall together; duration about five months; cause of death, cerebral embolus.
40	My case	M. 47.	None.	Right side.	Mixed, round and spindle cells.	Involved.	In lungs.	Compression of trachea; duration about 17 months.

Family history.—No. 13, none of malignant disease; 14, both mother and aunt had a goiter; 24, father had a goiter; 35, mother had a goiter.

Of the a
of previ
enlarge
where fi
afflicted
that in
definite
it is pr
a benigi
larger t
nign en
sarcoma
stateme
present.
ious goi
One car
Braun
cases in
Howeve
cases ar
tions ar

The
ance. I
the rem
expecte
goiter a

That
in adva
all obse
says th
strong
at a m
forty c

We thus see that an overwhelming majority of the cases occur after the fortieth year, with comparatively the largest number during the fifth decade. To give an adequate and satisfactory explanation for the occurrence of sarcoma in this location, at such an advanced age, contrary to what is usual—namely, the occurrence of sarcomata elsewhere at an earlier age—is, at the present state of our knowledge of neoplasms, impossible. However, we know from the researches of Wölfler that very frequently the parenchymatous elements of the thyroid become atrophic in later life, this atrophy being often accompanied by a copious hyperplasia of the interacinous connective tissue. Whether the pathologic mesoblastic tissue growth which forms the sarcoma is akin to the normal connective-tissue hyperplasia, or an exaggeration of the same, is perhaps an interesting speculation, but a question which must possibly remain unanswered until more is known of the physiology of the thyroid and the etiology of tumors in general.

The tumor more frequently originates in the right lobe of the thyroid than in the left. This is apparent from the examination of the appended table, and is also borne out by the statement of Lücke, that usually only one lobe of the gland is affected, and in the cases observed by him, the right lobe was the one involved. Family history of goiter, or of malignant disease, seems to be an unimportant element in causing a predisposition, being present in only a few cases; neither does previous injury to the thyroid gland appear to be an exciting factor of any moment.

The rate of growth of sarcomata of the thyroid is usually rapid, which may perhaps be explained in part by the copious blood-supply which this gland normally receives. The duration of the disease is somewhat difficult to establish exactly, for here dependence must be placed on the anamnestic statements of the patient, who may have for a short time overlooked a small tumor.

Lücke states that the duration of the disease appears not to be over one year. Indeed, so rapid and malignant is the course of these tumors that it leads Kocher to remark, "The more our experience with neoplasms of the thyroid gland increases, the more we come to the conclusion that this organ, aside from the bones, is relatively the most frequent seat of acute sarcomata, which, by means of their rapid development, may very easily be confounded with an acute inflammation."

In those histories which give sufficient data to establish the duration with approximate accuracy, the shortest time was four weeks, the longest seventeen months. A duration of perhaps six to seven months may be considered the average. The cause of death in a large number of cases is interference with the vital functions of respiration or deglutition, due to pressure on the trachea or esophagus. Death has also frequently followed closely after operation for removal of the neoplasm, from suppuration, asphyxia, bronchopneumonia and from secondary hemorrhage.

In size, the neoplasm varies from a nodule as large as a walnut, to a tumor filling up the entire anterior surface of the neck, from the hyoid bone above, to the sternum below. The contour is more or less irregular, the surface apt to be nodular and uneven. The consistence may be firm, or fluctuation may be obtainable on parts where the tumor tissue has broken down and become changed to a semifluid, or fluid detritus. The skin covering the tumor may be freely movable and unaltered, or it may be adherent and show the secondary changes due to invasion of its substance by sarcoma cells and subsequent ulceration, although this latter complication is not frequent.

In the early period of its development, the new growth is confined within the capsule of the gland, this condition being present at the time of operation in the case which I observed; but later its confines

are passed by the tumor cells and the neighboring tissues are invaded. When the tumor is large, the sternomastoid, sternohyoid and sternothyroid muscles are displaced, thinned, and their fibers separated by the pressure exerted by the tumor, while in some cases the muscle substance is infiltrated by the tumor tissue. (Case 25.)

The trachea, from its intimate relation to the thyroid gland, is one of the structures most frequently involved by the advance of the tumor growth. It may be dislocated toward one side or the other, bent and distorted. Pressure first produces a partial, later perhaps an almost complete obliteration of its lumen, while adhesions between its wall and the new growth rapidly form. Later the tumor cells frequently invade the walls of the trachea, which have become atrophic from pressure; then finally the mucous membrane is perforated and the tumor cells may continue their growth, forming a mass which projects into the tracheal lumen. (Case 25.)

Pressure on and invasion of the esophagus may occur in a like manner, but this complication is perhaps a little more uncommon than the condition just described. The larger vessels of the neck are frequently adherent to, or more or less completely surrounded by the tumor mass. Their lumen may be patent, or as is often found, the wall of the vein is infiltrated by embryonic cells, and its lumen filled by a thrombus, which may also in turn be invaded by the advancing sarcoma. The extent of this complication is well illustrated by a case described by Wölfler (Case 25.) The wall of the internal jugular was broken through by the tumor, on a level with the third ring of the trachea. Within the vein the tumor mass extended downward into the left innominate vein, and from here into the vena cava superior, projecting from the termination of this vein with a conic extremity into the right auricle. Upward

the tumor mass extended into the left facial vein and into the left sigmoid sinus.

The nerve trunks of the neck seem to resist for a long time the advance of the embryonal cells into their substance, nor is there often a disturbance of their function, though entirely surrounded by tumor tissue. That the nerve trunk may however be invaded, is shown by the case described by Mathieu. (No. 15 in the table.) The pneumogastric nerve was found to penetrate into the tumor mass and here showed double its normal volume. Microscopically, an infiltration of the nerve trunk by sarcomatous tumor elements was found, the bundles of nerve-fibers being pressed apart and separated from each other by the embryonic cells.

The cervical lymphatic glands are involved in a large number of cases. As shown by the appended table, the cervical glands were affected by the disease in eighteen of the forty cases. The study of the involvement of the cervical lymphatic glands is of importance, not only from a clinical standpoint in the differentiating between a benign and malignant goiter, but also from the point of view of the pathologist, because it teaches us, as Braun points out, one of the ways by which a tumor increases in size, and also how these tumors so completely surround the trachea, esophagus and great cervical vessels. Braun made serial transverse sections of the neck in a case of sarcoma of the thyroid, with very interesting results, coming to the following conclusion: "It is usually taken for granted that these rapidly growing neoplasms perforate the more or less resistant connective-tissue capsule which at first surrounds them, and after this has occurred, grow about and surround and press aside the trachea and esophagus. Certainly, however, increase in size of the thyroid tumors occurs as often, if not oftener, in the following manner: the primary tumor coalesces with the neighboring tumors, which in part may have originated from infected lymphatic glands,

and in part are metastatic nodules." Thus the trachea, the esophagus and also the large cervical blood-vessels become surrounded by tumor masses. This statement is illustrated by the case which I examined, where a process of the tumor passed behind the esophagus (v. s.). This extension was most probably formed by an infection of a retro-esophageal gland with tumor cells, with subsequent enlargement, and later a conjunction with the primary tumor.

The macroscopic appearance of the tumor on section is somewhat variable. As a rule, the cut surface is slightly moist, smooth, transparent (Kaufmann) or translucent and glossy. Kaufmann avers that "these tumors are differentiated by scattered bundles of fibrous tissue which course from the periphery toward the center of the tumor."

The morphology of thyroidal sarcomata has received a careful study from a number of investigators. An analysis of the cases which I have collected from the literature and the two cases reported herewith gives the following results:

1	Round-celled sarcomas	10
2	Spindle-celled sarcomas	6
3	Mixed-celled sarcomas	7
4	Alveolar sarcomata 1	
	" " and stellate cells 2	
	" angiosarcomata 2	5
5	Angiosarcoma	1
6.	Fibrosarcomata	3
7	Spindle cells with bony tissue	2
8	Cystosarcoma	1
9	Cavernous sarcoma	1
10	Angiosarcoma	1
11	Lymphosarcoma	1

This analysis shows: 1, the relative frequency of the round-celled sarcoma, which corresponds with the clinical observation of the rapid course of these tumors; 2, the relative infrequency of the fibrosarcoma, which is usually a somewhat more slowly growing tumor; 3, the relatively frequent occurrence of alveolar sarcomata; 4, the total absence of pigmented growths. From

which of the connective-tissue elements of the gland these tumors originate can not be definitely stated. Limacher describes one case in which the histogenesis of the sarcoma cells could be distinctly traced to the endothelial cells of the blood-vessels of the glands.

The manner of growth of the tumor and its effect on the normal or strumous thyroid are of interest. It was Kaufmann who called attention to the fact that the sarcoma cells invade the thyroid tissue by growing into the interacinous connective tissue, and by increasing in number, bring this to atrophy and gradually replace it. The pressure on the acini by the growing cells causes a compression, an atrophy and disappearance of the gland tissue proper. The interstitial development of these sarcomata has been emphasized by others, and Kaufmann asserts that it must be regarded as a rule.

The secondary changes which occur in sarcomata of the thyroid appear to be no different from those occurring in sarcomata elsewhere in the body. Ulceration appears to be a somewhat unusual complication, probably for the reason that death occurs from one of the above-mentioned causes, before atrophy and destruction of the skin has taken place, and infection of the thus exposed tumor tissue, with pus producing micro-organisms, can occur. In this connection, the case of Gatti is of interest. Suppuration occurred in the sarcomatous thyroid, with the formation of a small abscess, while blood examination revealed the presence of the streptococcus.

Sarcoma of the thyroid is one of the malignant tumors during the course of which metastases frequently form. Mestastasis takes place: 1, by way of the lymphatic vessels, as shown by the frequent involvement of the cervical and the occasional enlargement of the mediastinal lymphatic glands; and 2, by way of the blood-vessels, especially the veins. To emphasize this latter assertion, it is only necessary to recall the case of

Wolfler, just described. As may be noted by examination of the appended table, metastatic nodules were present in eighteen of the cases, or 45 per cent., exclusive of involvement of the cervical lymphatic glands. The distribution was as follows: Lung, 11; bones, 6; liver, 4; pleura, 3; heart, 2; mediastinal lymph, 2; dura mater, 2; intestines, 2; stomach, 1; pancreas, 1; kidney, 1; costal cartilage, 1; ant. mediastinum, 1; skin, 1; palate, 1.

As might have been expected, the primary metastases are most frequent in the lung tissue, and next to the lungs metastatic foci are found most frequently in the bones; having been present in 6 of the 18 cases in which metastases were found. This is equal to 30 per cent. Lücke gives the frequency of bone metastases in sarcomata which had produced metastases as 12.7 per cent., so it appears that bone metastases are 2½ times as frequent in sarcomata of the thyroid as in tumors of this class in general.

Limacher, as stated above, found 44 cases of sarcoma of the thyroid in the post-mortem records of the Berne Path. Institute, and among these 44 cases, 35 showed metastases. The difference between these figures and the figures deduced from the series of cases collected by myself is perhaps explained by the fact that in many cases, a post-mortem examination was not made, or if made, was not reported. So, very probably some metastatic foci have been thus overlooked. Among these 35 cases the distribution is as follows: Lung, 27; liver, 7; bones, 8; spleen, 1; brain, 3; heart, 3.

It will be noticed that in this series also, the metastases are relatively frequent in the lungs and in the bones. As far as my knowledge goes, no adequate explanation has been offered to account for this frequency of osseous metastases.

As the conclusions reached in this paper are based on the study of a comparatively small number of cases,

and as it is evidently not possible to enumerate all peculiarities and unusual manifestations of thyroidal sarcomata, it has seemed desirable to arrange in tabular form the chief facts of interest in the pathology of these tumors. Special care has been taken to include in this table several points concerning which there seems to be a difference of opinion among the various writers on the subject. An endeavor has also been made to bring out some of the salient points in the pathology of the disease, in each case, in order that a comprehensive picture of the many and various anatomic features might be presented.

In conclusion, I desire to express my sincere appreciation of the kindly interest and the help rendered by Prof. Ludwig Hektoen, in the preparation of this paper.

March 13, 1899.

REFERENCE.

1 Bircher: Sam'l Klin. Vortrage, No. 222, 1881.
2 Braun: Arch. f. Klin. Chirurg., 1879.
3 Bryant: Internat. Clinics, Phila., 1891, ii.
4 Doleris: Le Prog. Med., Paris, 1876, iv.
5 Ewaid: Nothnagel Spec. Path. u. Therap.
6 Forster: Wurzb. Med. Zeitschr., 1860, i.
7 Gratti: Revue de Chirurg., Paris, 1895.
8 Graham: Chicago Med. Recorder, 1893.
9 Heath: Med. Times and Gaz., London, 1879, ii.
10 Kaufmann: Deutsche. Zeitsch. f. Chirurg., 1879.
11 Kobler: Wiener Med. Woch., 1886, No. 9.
12 Kocher: Centralb. f. Chirurg., 1877, No. 45.
13 Lentz: Congres Franc. de Chirurg., Proc. verb. mem. et dis., 1893, vii.
14 Limacher: Virchow's Arch., Supp'l Heft. z. Bd., 151
15 Lucke: Handb. der allg. u. sp. Chir., von Pitha u. Biblioth., Erste abth., sechste lief.
16 Lucke u. Zahn: Chirurg. der Gesch., 1 Theil. Deutsche Chirurgie.
17 Mathieu: Le Prog. Med., Paris, 1881, ix.
18 Neumann: Langenbeck's Archiv., xxiii, 1879.
19 Pick: Zeitschr f. Heilk., 1892, xiii.
20 Pinner: Deutsche Zeitschr. f. Chirurg., 1882.
21 Raynaud: Bull. Acad. de Med., Paris, 1838-9, iii.
22 Pitt: Trans. Path. Soc., London, 1887.
23 Scheiber: Arch f. Path. Anat., Bd. liv.
24 Schmuziger: Cbl. f. Schw. Artzte, 1882.
25 Shattuck: Trans. Path. Soc., London, 1888, xxxix.
26 Stewart: British Med. Jour., 1879, i
27 Tilleaux: Bull. et Mem. de la Soc. de Chirurg. de Paris, 1881.
28 Turner: Trans. Clinical Soc., London, 1890, xxiii.
29 Virchow: Die Krank. Geschw.
30 Wolffler: Arch. f. Klin. Chirurg., 1883.

THE RESPIRATORY SYSTEM.

RHINITIS FIBRINOSA, INCLUDING A BACTERIOLOGIC AND HISTOLOGIC EXAMINATION OF CASES.

GEORGE L. CHAPMAN.

The subject of rhinitis fibrinosa is as a rule very briefly, if at all, treated in such text-books as might be expected to contain a detailed account of it. This disease was recognized and described by Fränkel, Hartmann, Seifert, and others. It is referred to under a variety of names, viz., croupous, membranous, fibrinous, primary pseudomembranous, plastic and fibrinoplastic rhinitis, and nasal diphtheria. Rhinitis fibrinosa is not a common disease; therefore, when observed, it deserves more than passing notice. It is characterized by an acute inflammation with a fibrinous exudate limited to the nasal cavities. The symptoms are usually benign, the most distressing being sudden nasal occlusion, necessitating almost constant oral respiration, mucopurulent discharge, and a somewhat chronic course.

The etiology of this form of nasal disease, as has been demonstrated by careful study, is not uniform. A few years after it had been generally recognized that the cause of a certain form of primary faucial diphtheria was the Klebs-Löffler bacillus, this micro-organism was looked for, and found to be present in a large percentage of the cases of rhinitis fibrinosa in which a bacteriologic examination was made. Concetti was the first to call attention to the contagious nature of the disease, and he recommended isolation and disinfection. The

first authors who undertook the bacteriologic examination of cases of rhinitis fibrinosa were Gradenigo and Maggiore. They claimed that the staphylococcus pyogenes aureus was the cause of the affection. Lieven isolated a staphylococcus which he claims is similar to the staphylococcus pyogenes aureus, but not identical with it. It is distinguished from the staphylococcus pyogenes aureus by some cultural features and by its lesser virulency. Abel did not find the diphtheria bacillus, but isolated pneumococci having a very mild degree of virulency.

Abbott reports three cases in which he found the diphtheria bacillus. His work is of special interest because of its thorough character. In two of his cases he found a bacillus similar to that of true diphtheria, but of lessened vitality. In the other case the bacillus found could not be differentiated from the typical diphtheria bacillus. M. Ravenel, in an investigation of ten cases, followed Abbott, and found in all but one a bacillus similar to the Klebs-Löffler bacillus, except for a lessened vitality and virulency. In one case, he found a bacillus which could not be differentiated from the true virulent, diphtheria bacillus. Bluder examined six cases, finding the diphtheria bacillus in all. Buys examined one case, finding the diphtheria bacillus. D. Braden Kyle reports two cases in which he found the staphylococcus aureus; he described the exudate as organized, laminated, fibrinoplastic.

The most extensive bacteriologic study of rhinitis fibrinosa was made by Meyer, who investigated thirty-one cases. He found that rhinitis fibrinosa may be caused by the diphtheria bacillus, but also by streptococci and staphylococci. In spite of the difference in the bacteriologic findings there was no material variation of the clinical course in his cases. In his excellent paper he calls attention to the fact that "a bacteriologic examination with reference to an exudate found in the nose

must of necessity be frequently misleading, since the nasal cavity is normally the habitat of a variety of microorganisms, among which is also found, occasionally in health, the diphtheria bacillus, which then may be obtained in culture without being the true cause of the disease."

Somers reports an interesting case in which the first culture did not show the diphtheria bacillus, though a subsequent culture revealed its presence. In this instance the disease was characterized by mild symptoms; although two other members of the same family became severely infected, one with laryngeal and the other with faucial diphtheria.

As is well known, a fibrinous exudate is frequently found after operations in the nasal cavity, especially after cauterization of the turbinate bodies.

Experiments to artificially produce rhinitis fibrinosa in man have been made only by Lieven, who, as stated before, claims that a specific staphylococcus is the cause of this affection. His experiments, while carefully made under the supervision of Seifert in Würzburg, have not yet been confirmed by others.

In view of the uncertain character of a bacteriologic examination in rhinitis fibrinosa, it has not been made the main feature of investigation in the cases to be reported in this paper. It may be at once stated that the diphtheria bacillus was not found in any one of them. Recently the nature of the exudate in bronchitis fibrinosa has become a matter of controversy. Beschorner, and also Grandy, have lately claimed that in bronchitis fibrinosa the casts consist of mucin, while in two cases examined by Herzog, the fibrinous nature of the exudate was demonstrated. It therefore appeared of interest to study the exudate in rhinitis fibrinosa to determine, if possible, its true nature. A satisfactory histologic examination can not be easily made in each and every case;

since it is difficult to obtain from the nasal cavity a piece of the pseudomembrane without crushing it in such a manner that it becomes useless for examination purposes.

Case 1.—R. J., male, aged 6 years, was brought to the nose and throat department of the Chicago Policlinic, Dr. M. R. Brown's clinic, October 4, 1897, complaining of nasal stenosis. The patient's temperature was normal. On examination, a dirty-white membrane was found, occluding both nasal cavities. The membrane exended over both the turbinate bodies and septum, beginning anteriorly about the mucocutaneous margin, and extending posteriorly, but limited to the nose. The boy's mother stated that he was restless and feverish at night, and had some discharge from the nose. On further inquiry it was found that the patient had had diphtheria some two years before, and that an older child was just recovering from an attack of sore throat—in all probability a follicular tonsillitis. The family was a large one, but there was no further contagion. A raw and bleeding surface was left upon the removal of a portion of the membrane for cultural purposes. A clinical diagnosis of rhinitis fibrinosa was made, and the following treatment instituted: Internally, an iron tonic, and locally, an alkaline cleansing wash, followed by insufflation of nosophen. The disease continued about three weeks, with more or less mucopurulent discharge. On examination of the culture a large staphylococcus was found. Its growth on agar-agar at ordinary room temperatures was dry, having a ragged margin and a distinct fetor; on gelatin, liquefaction was produced.

Case 2.—M. M., male, aged ten years, came under observation, October 11, 1897, suffering from nasal trouble. On examination a dirty-white membrane was found, anteriorly covering the septum and turbinate bodies. The posterior rhinoscopic image showed a similar condition, with a moderate hyperthropy of Luschka's tonsil. The membrane was confined to the respiratory region of the nasal mucous membrane as in the former case. A raw and bleeding surface was left upon the removal of a portion of the membrane. The submaxillary and cervical lymph-glands were swollen, simulating the collar of brawn of scarlet fever, but were not tender. The swollen condition of the glands continued about three weeks. The temperature was slightly elevated (99° F.), and the mother of the patient stated that he had been feverish and restless at night and had complained of some frontal headache during the previous three or four days. Most of the distress was caused by the nasal stenosis. The history revealed no immedately preceding sickness which would account for the trouble. The illness continued benignantly, with a mucopurulent discharge,

for about four weeks. No history of contagion could be obtained, although the patient was in almost constant contact with a brother. A clinical diagnosis of rhinitis fibrinosa was made, and treatment instituted as in the former case. The following day the patient returned for a bacteriologic examination. The membrane in this case was fortunately very readily removed with very slight hemorrhage, and cultures were made. The culture on agar-agar showed a staphylococcus and a species of saccharomyces. The growth on gelatin did not cause liquefaction.

Of the membrane obtained in this case, part was at once transferred to absolute alcohol; another part, without being subjected to any other treatment, was exposed to the action of dilute acetic acid, and a third portion, to that of artificial gastric juice. Dilute acetic acid caused the membrane to become almost perfectly transparent; at the same time there occurred on carefully shaking the test-tube without breaking up the membrane a very slight turbidity in the fluid. The result of this experiment showed that the membrane largely consisted of fibrin mixed in some way with a small amount of mucus. Exposed to the action of artificial gastric juice, the membrane within a few hours was almost completely digested. There remained only a very small, hardly appreciable, amount of undigested residue. This likewise proved the fibrinous nature of the exudate. The piece of membrane hardened in alcohol was subsequently embedded in paraffin and sectioned. The sections were studied with Gram's, Weigert's, Altmann's, and a hematoxylin stain. The mass of the exudate, as shown by the study of the sections, consisted of numerous, mostly polymorphonuclear leucocytes, a few epithelial cells, some cocci, and some indefinable débris; all of these elements were embedded in a dense fibrillar network. This network stained violet with hematoxylin, a beautiful blue with Weigert's fibrin stain, and red with Altmann's acid-fuchsin picric-acid stain.

Case 3.—T. C., male, ten years, presented himself for treatment. November 26, 1897; temperature normal. On examination a dirty-white membrane was found covering the septum and turbinate body of the right nasal cavity only; there was also present a deflection of the septum to the right. The patient's mother stated that he complained of some nausea and had a slight fever three days before, and was also greatly distressed because of the limited amount of nasal respiration permitted, which made him restless at night. Pieces of the membrane were removed, leaving the characteristic raw and bleeding surface. There was no history of contagion and no further symptoms of importance developed except a more or less mucopurulent discharge, the case continuing benignantly. A clinical diagnosis of rhinitis fibrinosa was made in this case, and similar treatment applied as in the previous cases. From the mem-

brane removed cultures were made and a staphylococcus found. The growth of the staphylococcus on agar-agar was moist and somewhat yellow. On gelatin, an extensive liquefaction was produced. Only small pieces of the membrane could be obtained in this case, but enough was secured to make the chemic tests, and a small part was hardened for sectioning as in the preceding case. Dilute acetic acid caused the membrane to become almost transparent. Artificial gastric juice caused an almost complete digestion within a few hours, with only a small amount of residue. The mass of the exudate was again proved to consist of numerous polymorphonuclear leucocytes, a few epithelial cells, cocci, and some indefinable débris, all embedded in a dense fibrillar network. This network stained blue with Weigert's and red with Altmann's stain. The stains employed, as well as the chemic tests, proved beyond a doubt that the great bulk of the exudate, as in the previous case, consisted of fibrin.

In conclusion, it is my agreeable duty to sincerely thank Dr. M. R. Brown for permission to publish these cases from his clinic, and also to thank Dr. Maximilian Herzog, director of the Pathologic Laboratory of the Policlinic, for his assistance and direction in the examinations.

Dec. 3, 1897.

A CASE OF PRIMARY TUBERCULOSIS OF THE LARYNX.

F. W. BULLEN.

The patient, a schoolboy aged 14, was admitted to Dr. Herrick's ward at Cook County Hospital on the 12th of last June. He was born in Germany and had lived in Chicago seven years. His parents were both living and well, and his family history was negative as far as known. He had always had poor health and had been in the hospital twice within the last two years with some acute trouble which he said was very similar to the present attack.

A week before entrance patient noticed a soreness in the throat and a slight dyspnea. The dyspnea had been gradually increasing in severity up to the time of admission to hospital, when he had some dysphagia, soreness in throat and complained of a feeling as though he was going to choke at times. He also had a harsh, painful cough, severe headache, and could

not speak above a whisper. He was weak and emaciated, countenance pale, expression anxious, lips cyanotic, mentality good. His temperature was normal: pulse 120, small and weak; respirations 30. His breathing was labored, the nares dilating widely and the soft parts of the chest retracting during each inspiration. The respiratory excursions were of equal volume on each side. The chest was narrow and the lower part of the sternum prominent. There was a left lateral scoliosis of three centimeters in the upper dorsal region. The lymph glands were enlarged and easily palpable in the neck, axilla, groin and cubital region. The percussion note over both lungs was hyper-resonant, and many sibilant and a few moist râles could be heard on both sides, anteriorly and posteriorly. The second pulmonic sound was accentuated, but no adventitious cardiac sounds could be heard. The tongue was very rough and slightly coated. The tonsils were hypertrophied and the mucous membrane of the pharynx injected. The vocal cords, as seen by the laryngoscope, were normal, but the soft tissues of the larynx appeared edematous. No false membrane was visible in pharynx or larynx, and the epiglottis was apparently absent.

The patient grew rapidly weaker and the breathing more difficult. Intubation was done with some difficulty owing to the condition of the tissues of the base of the tongue, but it did not relieve the dyspnea, so tracheotomy was done immediately and artificial respiration kept up for some time; but the patient could not be revived. The tracheotomy relieved the dyspnea, but the patient died apparently from exhaustion.

The autopsy was made twenty hours after death. The body was emaciated and the rigor mortis marked. There was a left lateral scoliosis of three centimeters; also a pectus carinatus of a moderate degree. The upper surface of the tongue was rough, and a deep, healed fisssure extended along the upper surface near the median line. The epiglottis was absent, except for a small irregular projection one-half centimeter in length at the left side of the base of the tongue. The lymph follicles at the base of the tongue were enlarged. There were several small ulcers in the mucous membrane of the pharynx, ranging in size from a pin-head to a split pea. The ulcers were shallow and nearly symmetrical, with smooth, even edges. On the posterior wall of the larynx below the vocal cords, extending down the trachea about three centimeters, was an irrregular papillomatous growth velvety to the touch, projecting about one centimeter above the mucous membrane. At the junction of the larynx and trachea it extended nearly around the entire circumference. There were a few ulcers in the larynx and upper portion of the trachea similar to those in the pharynx. The mucous membrane of the larynx and trachea was injected. The vocal cords were normal. There

was a tracheotomy wound in the median line involving the three upper rings of the trachea.

The lungs together weighed 480 grammes. The posterior surface of both lungs was covered with old fibrous adhesions. Several nodules, varying in size from a hazelnut to a hickory-nut, could be felt in both lungs, but were more numerous in the lower part of the left upper lobe. The lungs floated in water and crepitated, except over the nodules. The cut surface was a bright pink color, except through the nodules, which were grayish-white and the cut surface of which was granular. The apices were free from these nodules or from anything resembling a healed tubercular process. A purulent fluid could be expressed from the bronchi. The peribronchial lymph glands were enlarged to the size of a bean and quite firm, the cut surface being a brownish-red color. They contained no areas of necrosis. The heart was negative. The tunica intima of the thoracic aorta was a yellowish-white color and contained many raised white patches.

The kidneys together weighed 150 grammes. The capsule was smooth and peeled readily, but some of the kidney substance was removed with it. The cortex was swollen and bulged slightly on section; the cortical markings were distinct. The liver weighed 920 grammes, and its surface was smooth but mottled. It cut with slightly increased resistance. The lobular markings were indistinct, the lobules being apparently made up of a yellowish-white center and a dark red periphery. There was no amyloid change in the liver or spleen. The intestines were entirely negative. The mesenteric and retro-peritoneal lymph glands were slightly enlarged but otherwise negative.

Sections for microscopical examination were taken from the larynx, base of the tongue, lungs, liver, spleen, kidneys, heart, and cervical, peribronchial and mesenteric lymph glands.

The sections from the larynx were taken from the lower portion, where the granulation tissue was the thickest. It showed a subepithelial infiltration of lymphoid cells, amongst which were epithlioid and giant cells. Retrograde changes were beginning, as there was a fragmentation of the nuclei and areas of coagulation necrosis. Tubercle bacilli were demonstrated in the tissue by staining with carbol-fuchsin. The section through the base of the tongue showed a similar pathological structure, but contained in places cicatricial connective tissue. The sections from the lungs were taken through the small nodules. These nodules were found to be areas of bronchopneumonia in which were giant cells and areas of beginning necrosis. The liver contained numerous areas of lymphoid cells, located chiefly at the periphery of the lobules, and in one of these round cell areas was found a typical giant cell. The liver contained a large amount of pigment. The spleen also contained an excess of pigment, but was otherwise negative. The

changes in the kidney were those of an acute diffuse nephritis, the changes being most marked in the convoluted tubules. There was a pigmentation of the peribronchial glands, but none of the lymph glands showed any signs of tuberculosis although numerous sections were examined.

The anatomical diagnosis arrived at was as follows: 1, primary hypertrophic tuberculosis of the larynx with tubercular ulceration of the pharynx, larynx and trachea; 2, acute tuberculous bronchopneumonia; 3, acute bronchitis; 4, miliary tuberculosis of the liver; 5, acute diffuse nephritis; 6, old adhesive pleuritis; 7, atheroma of the thoracic aorta; 8, left lateral scoliosis; 9, tracheotomy wound of the trachea.

The case was thought to be one of hereditary syphilis developing at puberty, until the microscope demonstrated the tubercular nature of the lesions. Yet the tubercular infection may have been ingrafted on an old syphilitic lesion. The tubercular infection evidently began in the larynx, as the involvement here was much more extensive than elsewhere, and the changes were such that they must have preceded those in the lungs and liver. The lungs, glands and intestines were examined very carefully for tubercular foci, but none were found. The areas of bronchopneumonia were small and widely distributed, and were probably caused by the inhalation of small particles of tubercular tissue from the larynx. The infection of the liver probably occurred by way of the blood, as no foci were found in the intestines or mesenteric glands. The nature of the cicatricial changes at the base of the tongue could not be determined, but may have been syphilitic. The dyspnea was evidently caused by the hyperplastic character of the laryngeal tuberculosis, aided by inflammatory changes in the larynx and lungs.

November 8, 1897.

LYMPHO-SARCOMA OF THE MEDIASTINUM.

WITH INVASION OF THE PERICARDIUM, LEFT AURICLE, AND LEFT LUNG, CAUSING STENOSIS OF LEFT BRONCHUS AND PARALYSIS OF LEFT VOCAL CORD.

EDGAR P. COOK, JR.

The true pathologic condition in the following case was first recognized at the autopsy. The lesion belongs to a group in which the physical signs are often misleading and the clinical diagnosis surrounded by many difficulties. The case is therefore interesting in its bearing on the clinical diagnosis in allied cases as well as on account of the unusual post-mortem findings.

The clinical history is as follows: W. R., male, white, aged 27 years, native born, and a switchman by occupation, was admitted to the Cook County Hospital April 26, 1897, and assigned to Dr. Edwards' service. His complaint had begun eight months previous with sharp pains in the left side of the chest and a cough, which was accompanied by scanty expectoration. He had spit blood a few times. The pains in his side had been more or less persistent since the onset of the attack, and the cough was still aggravating, although practically unproductive. He had lost considerable flesh. The family history was negative, especially regarding lung disease. He had previously enjoyed health, but had drank freely and used tobacco. No history of venereal disease was obtained.

On physical examination the patient was found to be poorly nourished and anemic looking. He was mentally clear. The eyes were normal and the tongue clean. The chest was well developed. There was a slight fulness of the left side, and the respiratory movements were restricted. Over the left side of the chest, and chiefly over the lower half and posteriorly, there were dulness on percussion and loss of vocal and tactile fremitus. The breath sounds were absent except at the apex, where the breathing was tubular in character. The right lung was negative on percussion and auscultation, and the respiratory excursion was normal. The area of cardiac dulness began above at the second interspace; the right border was at the right sternal line, and the left border could not be made out, as the area of cardiac dulness merged into that over the left lung. The apex beat was seen diffuse inside the left nipple line, and the impulse could be distinctly felt over the xiphoid cartilage. There was a low, harsh, systolic murmur at the apex, and a

slight duplication of the second sound was noted toward the base. The abdomen was negative. The spleen was not palpable. The area of liver dulness was normal above but extended nearly two inches below the costal arch. There was no tenderness in the hepatic region. The extremities and genitalia were negative. The superficial lymphatic glands were not enlarged. The sputum was very scanty, and repeated examination showed absence of tubercle bacilli. The urinalysis was negative. Exploratory aspiration of the dull area on the left side of the chest resulted in a dry tap.

The patient remained in the hospital from April 26 until May 31. The temperature curve during this period was of an irregular type, the temperature ranging about normal as a rule, but occasionally rising to 102.8° to 104° F., without apparent cause, the pyrexia persisting only a short time. The fever was never of a true intermittent type, and there were no chills.

The patient was discharged May 31, 1897, with a diagnosis of chronic tubercular pleurisy. He re-entered the hospital about three weeks later, on June 19, complaining of attacks of dyspnea, which had begun shortly after he had left the hospital and were rapidly increasing in frequency and severity. The patient now presented in addition to the condition described above a marked loss of voice, being unable to speak above a hoarse whisper. He suffered from attacks of severe dyspnea, during which he sat with his head and chest thrown forward, the chest being flexed upon the abdomen. He could not rest in the recumbent posture. The respirations were wheezing at times and accompanied by a dry, brassy cough. The dyspnea was chiefly inspiratory and there was some retraction of the soft parts of the chest. The accessory muscles of respiration were in constant play, and the anxious expression, the cyanosis, and the cold sweat, which bathed the patient in his struggle for breath, all combined to make a picture pitiable indeed. Morphin alone afforded relief during the attacks, and hot moist inhalations were of temporary value. There was slight dysphagia. The laryngoscopic examination revealed a normal larynx, except that there was a complete paralysis of the left vocal cord corresponding to that due to some lesion of the recurrent laryngeal nerve. Intubation was considered, but discarded on account of the obstruction being clearly infralaryngeal.

The patient died rather suddenly June 29, 1897, just after a severe dyspneic attack. The temperature rose rapidly from normal to 103.8° F. shortly before death. The ante-mortem diagnosis was chronic tubercular pleurisy (left), with paralysis of the left vocal cord, probably due to the tubercular process invading the mediastinum and involving the left inferior laryngeal nerve, either by pressure of enlarged glands or inflammatory bands.

The autopsy was held fifteen hours after death. Body male; poorly nourished. Abdominal cavity empty; peritoneum smooth. Right pleural cavity free from adhesions and fluid; left pleural cavity obliterated by firm old adhesions. Pericardial cavity contained a few easily broken fibrinous bands and several ounces of turbid, yellowish fluid containing a few flakes; the wall of the pericardium partly covered with masses of fibrin; at its base was a circular projection into the cavity measuring six centimeters in diameter. Larynx and trachea filled with mucus; tracheal mucosa and vocal cords normal. Left bronchus stenosed at its beginning from pressure of tumor masses outside; it barely admitted little finger; right bronchus normal. Fifteen centimeters below epiglottis there was a nodular projection into esophagus from tumor outside. In front and at root of left lung was a large nodular tumor of size of fist projecting into pericardium from behind. The heart lay in middle line of chest in front of tumor; it weighed 400 grammes; numerous granular fibrinous masses were found over base, chiefly over right auricle. In removing the heart the left auricle was opened into and tumor mass found adherent to posterior wall and projecting into cavity of auricle. Tumor mass was continuous with pericardium and projected one centimeter into left auricle; it was white, smooth, lobular, of the size of a walnut, measuring 2.5x3 centimeters, and containing few ecchymoses. On section tissue was uniform, soft, and vascular; a thin, milky fluid exuded on pressure; there were no points of ulceration or necrosis. Aortic and pulmonary valves were normal and competent. Right heart was filled with dark clotted blood. Tricuspid and mitral valves negative; endocardium negative; myocardium flabby, uniform, light-grayish red. Beginning of aorta studded with minute grayish areas; diameter two centimeters at four centimeters above valves; coronary orifices patent; thoracic aorta smooth. Left lung showed greatly thickened pleura. In lung substance were numerous cavities containing thick, brown, purulent material; intervening lung substance was gray, non-crepitant, and contained much fibrous tissue. Cavities were most numerous below. Posterior part of lung was invaded by tumor tissue in nodules more or less spherical. Tumor tissue on section was light gray and contained milky fluid. In places it was very vascular and in others yellowish. Peribronchial glands of left lung were pigmented but not enlarged. Right lung normal; no changes in apex. Spleen negative. Kidneys together weighed 300 grammes. On convex border of right kidney was a small rounded whitish nodule of size of split pea, extending 0.5 centimeter into kidney substance. Liver weighed 2100 grammes; it was somewhat pale in places, but lobular markings were well preserved. On upper surface of left lobe was a whitish nodular mass of size of split pea, and a second umbilicated circular

nodule two centimeters in diameter; on under surface of left lobe was a similar nodule three centimeters in diameter. Nodules on section exuded a milky substance and corresponded otherwise to tumor previously described. Other abdominal viscera showed nothing of importance.

Anatomical diagnosis: Lympho-sarcoma of mediastinal glands, extending into pericardium, left auricle, and left lung, and causing stenosis of left bronchus; chronic adhesive pleuritis (left); multiple abscesses of left lung; fibrinous pericarditis; metastatic nodules in liver and kidney; follicular enteritis: mucous colitis.

Histological examination: Microscopical examination of sections from the tumor showed it to be composed of masses of small round cells lying in a coarse reticulum. It was a typical small round-celled sarcoma.

It will be noted that the tumor mass, lying posterior to the heart, which was flattened out, as it were, in the median line of the chest, was not accessible to the ordinary means of diagnosis. The physical findings in the left side of the chest corresponded well with a chronic pleurisy with great thickening of the pleuræ, and the absence of appreciable expectoration made it impossible to recognize the condition of multiple abscess formation present in the lung. In addition, the negative result from an exploratory aspiration seemed to confirm the diagnosis of pleural thickening. The paralysis of the left vocal cord and the peculiar dyspneic attacks were attributed to some pressure on the left recurrent laryngeal nerve and left bronchus, but an extension of the tubercular process, especially a tubercular involvement of the mediastinal glands, was thought to be the most probable cause. Aneurism of the aorta was excluded on the negative circulatory signs and the absence of expansile tumor. A malignant growth of the mediastinum was overlooked because the chronic pleurisy seemed to be the primary lesion, and the paralysis and dyspnea were thought to be explainable on the ground of a secondary extension of the inflammatory process to the mediastinum. As the autopsy proved, however, the mediastinal tumor was the primary lesion, and the lung disease was a secondary condition arising from the obstruction of the bronchus.

November 8, 1897.

SUDDEN DEATH FROM PULMONARY EMBOLISM FOLLOWING THROMBOSIS OF THE INTERNAL JUGULAR VEIN.

LUDVIG HEKTOEN.

The following post-mortem of a case of sudden death is reported without comment, as an additional striking example of unexpected, practically instantaneous death from embolism of the main stem of the pulmonary artery.

A woman, 67 years old, was operated on for carcinoma of the left half of the tip of the tongue—partial excision—one year previous to admission into the service of Dr. Charles Adams, in the Cook County Hospital, on account of a secondary infiltration in the tissues of the left side of the neck. On Nov. 6, 1898, this mass was removed by a painstaking dissection, during which the large vessels of the neck were laid wholly bare. The patient recovered readily from the operation and anesthesia, and seemed to be doing very well for the following twenty-four hours, at the end of which, and without any warning, she suddenly became cyanotic and expired. The agony lasted perhaps one minute or so, according to Dr. Low, who witnessed the final scene. The post-mortem was made before a class of students forty-eight hours later.

Anatomical Diagnosis: Partial excision of tongue, healing; recent extensive dissection on left side of neck; parietal thrombosis of left carotid artery; thrombosis of the left internal jugular vein; embolism of pulmonary artery; bloody hydropericardium; chronic granular pericarditis; arteriosclerosis (minimum degree); bronchitis; adhesive pleuritis; chronic nephritis; fibromyoma of uterus.

The body is that of an old, well developed, fairly well nourished woman; rigor well marked; usual posterior lividity.

In the skin of the left side of the neck, along the anterior margin of the sterno-cleido-mastoid muscle, runs a recent, sutured incision, 9 cm. long, which leads into an extensive cavity lined with a reddish-gray, velvety tissue and partly filled with moist strands of gauze, the ends of which emerge through two small openings in the skin of the back part of the neck. Along the floor of this cavity run the deep cervical vessels, which have been dissected free from their normal connections. The upper part of the internal jugular vein, which is distended, contains adherent, grey and granular thrombic masses; the lower part of the vein is empty. The internal carotid is rough in one place, over which there is a thin layer of fibrin.

The peritoneal cavity is empty and its lining smooth and free from adhesions. The right pleural cavity is empty, its lining smooth; the left pleural cavity is largely obliterated by firm, fibrous adhesions. The pericardium is distended with bloody fluid which does not contain any clots. There are no openings in any of the subpericardial vessels. The lining of the pericardium is rough and granular, due to firm, fibrous thickenings.

The stem of the pulmonary artery is distended; upon opening it two large, yellowish-gray, granular, rough cylindrical masses fall out; each is about 5 cm. in length and 2 cm. in the greatest transverse diameter; rolled up between these masses are fibrinous casts of smaller, dichotomously branching vessels.

The heart weighs 300 gms., the endocardium is smooth, the heart muscle rather loose in texture, free from interstitial changes; the coronary arteries are quite smooth. The beginning of the aorta is rather rough and contains yellowish raised areas and a few calcareous plates.

The lining of the pharynx, esophagus, larynx, and trachea is smooth. The left half of the tongue anteriorly shows an extensive loss of substance; in the contracted scar which binds this part to the floor of the mouth there is no sign of any tumor-growth.

Both lungs crepitate; their substance contains only a moderate amount of blood; in the bronchi is a small amount of muco-pus. The peribronchial lymph glands are prominent and black.

The spleen weighs 120 gms., and does not show any changes. The liver weighs 1450 gms.; there is a shallow furrow extending transversely across the two lobes of the liver, at the junction of their lower and middle thirds approximately. The liver is rather yellowish, of uniform consistency, and contains much blood. The gall-bladder and biliary ducts are normal. The pancreas weighs 80 gms.; the cut surface is normal. The stomach and intestines are also quite normal.

The kidneys weigh 250 gms., their capsules adhere, the cortex is deep-red, thinner than normal, and the cortical markings indistinct; the pelvis, ureters, and bladder are free from changes.

The left angle of the uterus, which is normal in size, contains a round tumor as large as a pigeon's egg, of firm consistency, whitish color, and a concentric fibrillated structure. The ovaries and tubes are normal.

The abdominal aorta and its large branches are quite smooth.

The brain and its membranes were not examined because of refusal of permission to do so.

Remarks: In conclusion the remark must be made that it is quite evident that the thrombus in the internal jugular vein had formed a considerable time before the

operation, most likely on account of the pressure of the surrounding tumor infiltration. Undoubtedly the manipulations of the thrombosed vein incident to the operation may have had something to do with the loosening of the mass that finally floated out into the circulation and on lodgment completely occluded the pulmonary artery.

November 14, 1898.

A CASE OF FIBRINOUS BRONCHITIS

JOSEPH M. PATTON AND MAXMILIAN HERZOG.

Chronic essential (primary) fibrinous bronchitis, croupous bronchitis or bronchitis pseudomembranacea is a rare affection. Its rarity is commented on by every observer of the disease, and is sustained by the small number of cases reported, no observer having seen more than one or two cases.

Birmer[1], who wrote the first extensive monograph on the subject, in 1855, says: "Bronchitis crouposa is a very rare affliction." Galen[2] observed a case of bronchitis fibrinosa, though he erroneously described the bronchial cast which he saw as a coughed up pulmonary blood-vessel. Tulpius[3] in 1641, presented the first reliable report on fibrinous bronchitis. He described the fibrinous exudate as *surculi venae arteriosae expectorati*, and illustrated his report by two drawings which do not leave any doubt as to the nature of the affection. Morgagni[4], in 1760, described fibrinous bronchitis.

Birmer (loc. cit.) gives an elaborate description of fibrinous bronchitis based on a series of fifty-eight cases, of which number fifty-six were collected by him from literature. Two cases came under Birmer's own observation.

An extensive monograph on fibrinous bronchitis, with a complete list of the literature pertaining thereto, is found in the chapter on this subject by Riegel[5] in Ziemssen's "Handbuch." In 1893 an extensive article was published by Beschorner[6] in which we find the first contradiction of the generally accepted view of the fibrinous nature of the exudate expelled in the form of bronchial casts in fibrinous bronchitis.

In the case reported by Beschorner the microscopic examination was made by Neelsen, who found that sections taken from the casts when stained according to Weigert's formula did not, as they should if composed of fibrin, display a blue color, but became a pale gray. Beschorner, therefore, maintains that the material from which the casts are formed is not fibrin but mucin, and he draws a parallel between the conditions found and the exudates formed in bronchitis fibrinosa and those in enteritis pseudomembranacea.

Similar conclusions are arrived at by Grandy[7], an American, who quite recently, under Weigert's direction, examined microscopically a case of bronchitis crouposa which came to post-mortem.

Grandy's report is as follows: Stains of sections from casts; no color with Weigert's stain for fibrin. With thionin there resulted a weak rose color, but formalin preparations do not stain well with thoinin. Sections from the bronchi: One can see distinctly how the exudate makes its way from the excretory ducts, and from there into the bronchi, that is into the bronchial exudate.

The exudate in the bronchi and the goblet cells give the reactions characteristic of mucus: *light blue* with Van Gieson's stain, *rose red* with thionin and rather dark brown with Bismarck brown.

Farther away from the walls of the bronchi the exudate was changed and did not show the characteristic stain. Thoroughly negative was the result with Wei-

gert's fibrin stain. The mass never stained a beautiful blue like fibrin would do, but invariably stained a pale gray like the ordinary tissue.

The results of the examinations of Beschorner, Neelsen and Grandy stand in opposition to the statement of Klebs[8], who maintains that the exudate in bronchitis crouposa is of a true fibrinous nature. Eppinger[9] expresses the same view as Klebs, and bases his opinion on the result which he obtained with Weigert's fibrin stain.

In the case which we can add to the list of cases of bronchitis fibrinosa already published, the result of the examination of the exudate is such that we must claim that the latter is of a true fibrinous nature and consists of true fibrin.

Unfortunately, chemic tests were not made while the exudate was fresh. Still, the tinctorial tests are so decided in their results that they leave no doubt as to the fibrinous nature of the exudate.

The clinical history of the case (presented through the courtesy of Clinical Assistant Dr. Gottschalk) is not as complete as could be desired, but as far as could be obtained is as follows:

Male, aged 40, married, beer bottler by occupation. Was perfectly well until two years ago, when he caught cold while working in a wet place. During the last two years he has had repeated attacks of bronchitis. These attacks would last a week or ten days, and were characterized by rather severe rasping cough. Expectoration was comparatively free, and there was no particular pain in the chest. About ten weeks before his recent attack he began to cough and expectorate large masses of tough, tenacious sputum, which was accompanied at times by some bloody expectoration. About four weeks before the expectoration of the cast, he developed high fever, great dyspnea and a distressing cough. There was diminished expansion and dulness over the lower two-thirds of the left lung as compared

with the right lung. This attack lasted between three and four weeks, and continued up to the time of the expectoration of the bronchial cast. During this period he was confined to bed and suffered with severe dyspnea, cough, and a temperature at times above 102 degrees F.

Three days ago he expectorated considerable blood. The temperature remained high and the dyspnea and cough distressing.

This morning he had a severe attack of dyspnea and coughing. Temperature rose to 104 degrees F. After considerable effort he expectorated a large mass of material which consisted of the bronchial cast mixed with mucus and quite a little blood. The temperature became reduced almost immediately, and the cough and dyspnea were relieved.

Within a very short time after expectorating the cast an examination, made by Dr. Gottschalk, showed that air was entering all parts of the left lung with comparative freedom. The percussion note was almost normal, and there were mucous râles to be heard over both lungs. The patient improved rapidly and all trace of him was subsequently lost, so that it is impossible to tell what his present condition is.

In view of the marked tendency of these exudations to recur, the subsequent history of this patient would be interesting, could it be obtained.

Pathologic report.—When the fibrinous casts were obtained, two tubes containing Lœffler's blood-serum mixture were inoculated at once and placed in the brood-oven for twenty-four hours. These tubes did not develop any diphtheria bacilli, but colonies, which consisted of large round micro-organisms, probably yeast cells or a species of torula.

The exudate as obtained consisted of a cast of the bronchial tree, of a total length of over 10 cm. Its main short stem, which is about 1 cm. long, is about as thick as a lead pencil and the branches run out to

fine filaments. They, however, do not all terminate in a very fine thread, but some, at their ends, show a dilatation which probably represents a cast of an infundibulum. The larger branches here and there show nodular prominences. The larger tube-casts, when examined in cross sections, show a more or less central lumen, and a lamellar structure of their walls. The ap-

Bronchial cast from case of fibrinous bronchitis.

pearance and make up answers to descriptions given before as to the structure of the casts in croupous bronchitis. The color of the casts is a gray with a tinge of brownish red.

Pieces of the casts were hardened in alcohol, and

also in formalin with subsequent alcohol hardening and stained according to different methods.

Bronchial cast from case of fibrinous bronchitis.

1. *Gram's stain.*—The following micro-organisms were found in sections stained according to Gram: Staphylococci, large bacilli with square ends (about 5 to 7 μ or more long) uniformly but slightly stained; smaller bacilli (3 to 4 μ) having stained very deeply;

small bacilli (2 to 3 μ) with rounded ends, which have not taken the stain uniformly; large spherical microorganisms looking like saccharomyces or torula.

2. *Weigert's formula for fibrin stain.*—The great bulk of the mass of the exudate which shows a fibrillar arrangement, stains beautifully blue, giving a typical fibrin stain.

3. *Hematoxylon.*—The great bulk of the tissue takes a deep hematoxylin stain.

4. *Van Gieson's* stain imparts to the tissue a reddish-brown color.

5. *Altmann's* acid-fuchsin picric acid stain for granula and fibrin produces a vivid red color.

From the enumeration of the stains used and the results obtained, it is evident that the casts consist of fibrin. Mixed with it are found swollen degenerating epithelial cells and a considerable number of leucocytes.

Optical test.—Small pieces of the casts, after hardening, were washed in distilled water and then teased on a slide and covered with a cover glass, and the effect was watched under the microscope. The tissue became somewhat transparent, though not very much so.

Chemical test.—Two decigrams of the hardened casts, after being well washed in distilled water and subsequently dried between filter paper, were subjected to the action of 10 c.c. of artificial gastric juice. After being in the brood-oven for three hours the exudate so treated had been completely digested. Mucin under these circumstances would not have been digested.

All the tests employed, therefore, had furnished results establishing beyond a doubt the fibrinous nature of the exudate expelled in our case of bronchitis crouposa.

October 11, 1897.

BIBLIOGRAPHY.

1. Birmer: Die Lehre vom Auswurf, Wuerzburg, 1855, and also in Virchow's Handbuch d. spec. Pathol., Vol. v, "Diseases of the Bronchi."

2. Galen: De locis affectis, Lib. ii, capt. i.
3. Tulpius: Observation med. Lib. ii, capt. xii, page 115, Amsterlodamia, 1641.
4. Morgagni: De sed et caus. morb. Epist. xxi, capt. xx, 1760.
5. Riegel: Ziemssen's Hanbuch, Vol. iv, pt. 2, p. 186, "Die Krankheiten des Respirationsappar."
6. Beschorner: Ueber chronische essentielle fibrinoese Bronchitis Volkmann's klin. Vortraege, 1893, No. 73.
7. Grandy: Ueber sogenannten chronischen Bronchial croup. Centralbl. f. Allgem. Pathol. Vol. viii, No. 13, July, 1897.
8. Klebs: Allgem. Pathol Jena, 1889, Vol. ii, p. 410.
9. Eppinger: Lubarsch and Ostertag; Ergebnisse der allgem. Path ologie, p. 200.

DISCUSSION.

DR. JOHN EDWIN RHODES—I have the pleasure of making a brief preliminary report to-night of a case of exudative bronchitis. Inasmuch as I saw the patient only yesterday, it has been impossible to prepare a chemical and bacteriologic examination of the exudate. This will be done, however, at a later date. The history in brief of the patient is as follows:

Mrs. M. A. H., daughter of Irish parents, born in Ohio, is 38 years of age and has been married eighteen years. Her mother is living at 62, healthy. Father died of cancer of the stomach at 50. One sister died of paralysis at 26. One brother died of typhoid fever at 22. One brother living, 26 years, good health. Five other children died in childhood; one of measles, one of croup, one was still-born. She has never been pregnant. Menstruation never regular; formerly had a vicarious nasal hemorrhage at each menstrual epoch; has not menstruated now for five years; has had two rectal abscesses—one last winter and one two years ago; one was lanced, the other opened spontaneously. They remained open for two or three weeks. Has usually had good health, but has never been rugged. Five years ago had an attack of typhoid fever of two months duration. For a period of two weeks last winter she expectorated casts similar to those here shown. Her present illness dates from May, 1897. She was seen shortly after this by my clinical assistant, Dr. I. Rasmussen, at the Northwestern University Woman's Medical School, shortly after this date. At this time she had swelling of the lower extremities below the knees, more particularly about the ankles. This was accompanied by an intense itching of the skin and was followed by eczematous eruption. At this time also cough developed. Diarrhea was present and she had suffered from this for a year previous to May, the movements of the bowels being loose, painless and sometimes ten or fifteen in number daily. She has been in bed now for two weeks; her appetite is very poor, and has been since May, and nourishment is now confined to liquid food, milk, and brandy, with an occasional egg and wine. The taking of solid food is followed by vomiting; has loss of about twenty-five pounds in weight. The patient has been addicted to the excessive use of stimulants for some months, which may

account for the loss of appetite and irritability of the stomach. About one month ago she began to expectorate casts from the bronchial tubes, and this has continued almost daily since. The cough is quite frequent, though usually much worse at night, quite dry, no yellowish expectoration. The casts are raised with difficulty, but as soon as they reach the trachea, they are expectorated easily. She thinks they start from an area about the lower substernal region on the right side. She has considerable dyspnea, especially marked just before expectorating the casts. This is relieved when the casts have been raised, as well as the wheezing respiration which is occasionally present. She has had continuous palpitation for many years, but this is not a marked symptom. She has had night sweats since May. At the present time her pulse is 100, regular and of moderate strength. Respirations 24, temperature 99 3/5. Tongue very red at tip, slightly coated. Her color is good, no marked emaciation; skin moist; cough, spasmodic, dry and frequent. As a whole her general condition is good and there is no great depression. On examination of the chest the heart is shown to be normal. In front there are no abnormal signs. Behind, in the subscapular region on both sides, there is slight dulness. On auscultation murmur seems harsh and a few moist râles are heard on inspiration in irregular areas, and are changed but not removed by coughing. The casts which I show you are rolled up irregularly when expectorated, and vary very much in size; they are of a grayish white color, and seem to have entirely filled the caliber of the tubes; they are evidently from several different areas. The patient is now under treatment and a further report will be made after she has been under observation for a longer time.

THE CIRCULATORY SYSTEM.

ABERRANT TENDINOUS CORDS OF THE HEART.

HENRY F. LEWIS.

In the cavities of the human heart are to be found numerous bands and cords of fibrous tissue stretching across the chambers and along the walls, some normal, some clearly abnormal, and others about which there might be question. There may be considered five varieties of such tendinous cords. First are those connecting the papillary muscles with the mitral and tricuspid valves and connecting these valves with points on the ventricular walls. The second are the short cords running along the muscular trabeculæ, chiefly in the lower part of the ventricular cavities. Both of these are normal and to be found in all hearts. In this connection let me make mention of the term "moderator band" often met in the works of English writers. Quain[1] says that a fibrous band, sometimes muscular, is often found stretching across the cavity of the right ventricle from the base of the anterior papillary muscle to the septum. This band is said to be always found in the heart of the ox and most other mammals—and in that of man may be taken to be analogous. M. Brown,[2] in an article on the structure of the mammalian heart, takes the ground that this band is normal also in man, stating that he never found it absent in 100 hearts examined by him, although only faintly marked in 15. He thinks its function is to pull the anterior papillary muscle toward the septum and thereby prevent insufficiency of the tricuspid when there is a tendency to overdistention of the right ventricle which may often occur physiologically.

I have not observed it in any marked form in any of the hearts which I have dissected, although there were in most of the cases short, fibrous cords about the bases of the papillary muscles of both ventricles and not particularly marked on the right side. Other English observers apply the term moderator band to any band or cord running across the upper part of either ventricle.

The aberrant cords may be divided into three classes: First are those often found running along the wall, usually of the ventricle, without any connection with the valve-curtains or the trabeculæ. Second are to be considered the cords or bands which stretch across the chamber from one wall to another or from a papillary muscle. These are said by most authors to be found only in the left ventricle,[3] but I have found them also in the right and a few have been reported in an auricle. This variety of aberrant cord is the one which may cause physical signs before death, namely, the high-pitched musical note heard during systole or at the beginning of diastole.[4] Third is a rare class of anomalous cords extending from the auricle into the ventricle, usually connecting the valve of the foramen ovale with a leaf of the mitral. I have met with no example of this kind and only a few cases are recorded [5], [7], [8]. Since this variety would be strikingly brought to the view of one performing an autopsy, it would not be so easily cut in opening the heart as the second variety. It is unlikely to be missed and would be more often reported unless very rare. I think that the cords of the other kinds are often overlooked because not in the mind of the operator and also because so easily cut in opening the heart.

In Professor Hektoen's laboratory of Rush Medical College I have dissected 80 hearts from the collection in the Pathological Museum. Some were the hearts of monsters, a few were abnormal only as to their tendinous cords, and the rest pathologic for various reasons; 51 show anomalous cords.

The monsters were one cyclops, one omphalopagus, and seven anencephali. The heart of the cyclops had a rudimentary pulmonary artery, an aorta arising from both ventricles, a defect in the ventricular septum, and a widely open foramen ovale, but no aberrant tendinous cords. The larger heart of the omphalopagus had no aberrant cords. The smaller heart had numerous short ones running along the walls of the left ventricle and several stretched across the lower half of the cavity of the same chamber. Of the anencephali, three exhibited no abnormal cords; one had several running longitudinally in the left and one such cord in the right ventricle; another had several similar cords in the left ventricle only; another had a few stretched across the cavity of the left ventricle near the apex and one across the middle of the right ventricle, with five branches at one end and connected at its middle with another cord running down to the apex; another had a thin muscular band running from near the apex of the left ventricle to the middle of the anterior papillary muscle of the mitral valve.

An analysis of the 51 hearts showing anomalous tendinous cords reveals some facts of interest: 32 in the left ventricle had abnormal bands of the second variety, viz., across the cavity of the chamber from one wall to another. In 12 of these cases there was more than one such cord, and some were branched or formed a network strung across the ventricular cavity. In 12 of the 51 hearts were one or more such fibrous or muscular bands across the cavity of the right ventricle; multiple in 5 cases. Six of the above hearts showed aberrant chordæ tendineæ of the second class in both ventricles. As examples of the first class, viz., tendinous cords running longitudinally from one point on the wall to another, there were 5 in the left ventricle, 3 in the right, and 1 in both. In 6 hearts there were one or more cords, or, more often, a network of fine fibers running vertically

across the opening of the posterior appendix of the right auricle. In 8 cases, in addition to the valve of the coronary vein (valvula Thebesii), or, in place of it, were thin cords singly or in network. Four hearts had bands or cords stretching between the papillary muscles.

Some of the cases may be worthy of more detailed mention. The hearts of the monsters have already been described. In one of the other cases there were numerous small transverse cords from the bases of papillary muscles in the left ventricle, and, in the right chamber, a muscle band 2 mm. thick diagonally across from the apex to the ventricular wall, with two tendinous cords running from it to other parts of the wall, also a network of three or four strands across the cavity of the ventricle. Another had, in the right ventricle, a muscular band 1 mm. thick, from a little below the pulmonary cusps across to the opposite wall, branching at one end, and also, in the left, a cord 35 mm. long diagonally across and upward from between the bases of two papillary muscles to a forked termination just below the aortic valves. Another showed several branching and coarsely meshed cords across from the base of one of the tricuspid papillary muscles to the ventricular septum, a sort of composite moderator band[2]. Another had, on the middle of the septum in the left ventricle, a muscular mass which received several branching cords from the apex and one long cord with two branches across from the left wall. In another heart a thick cord 20 mm. long, with two muscular branches, ran across the cavity of the left ventricle to join a longitudinal muscular band and so were reticulated masses, the latter especially numerous in the right ventricle. Chiari[8] describes a series of reticulated structures found by him in the right auricle and connected with the Eustachian or Thebesian valves. Such marked examples as he describes I have not seen, but several of the hearts examined by me showed a network of fibers across the opening of the

posterior auricular appendage of the right side, and others showed several thin cords or fenestrated membranes in place of the Thebesian valve or situated just beyond it and across the opening of the coronary vein.

Among my cases there was none showing a cord across the cavity of the left auricle. Apparently such are very rare. Fowler[9] in 1882 exhibited to the London Pathological Society a heart in the left auricle of which was a band from ¾ inch to 1 inch wide, containing some muscle-fibers. It was continuous with the membrane covering the foramen ovale and ran across the cavity of the auricle, to be blended with the endocardium, just beyond the opening of the auricular appendix, and between the inferior pulmonary veins. It appeared to be an overgrowth of the valve of the foramen ovale. The case occurred in a woman of 42, who died of carcinoma of the liver, without showing any cardiac symptoms. Before the Anatomical Society of Great Britain and Ireland, in 1896, were reported two similar cases, both without antemortem signs. [10], [11].

In considering the origin of aberrant tendinous cords of the heart the development of that organ must be reviewed. The endocardium, like the endothelial lining of the blood-vessels, probably arises from the entoderm. At least for a considerable time the endothelial heart is distinct and forms a sac by itself, inside the fibro-muscular portion of the cardiac tube. The latter grows inward, finally occupying and filling the interspace. The elongated, spindle-shaped cells of the embryonic muscular tissue of the heart are arranged in bundles running in different directions. Some of these bundles are closely packed together to form the walls of the different cavities, while others are more or less widely separated from each other to form the trabeculæ and tendinous cords, being covered and invested by the endothelial cells as the outer and inner sacs of the primitive heart finally coalesce. Before this coalescence

takes place the space between the mesenchymatous and endothelial portions is filled by a gelatinous layer through which the network of mesenchymatous fibers pushes toward the center. Thus, particularly in the ventricles, the cavity is nearly filled with a sponge-like mass of muscular trabeculæ[12]. The endothelium later becomes depressed between these bands and into the interstices, while the trabeculæ in general become arranged closer to the compact muscular tissue of the wall of the heart, except where they are developed into the columnæ carneæ, the papillary muscles and the tendinous cords. A mass of soft, thick tissue forms at the auriculo-ventricular orifice in the region of the septum intermedium and connected with the spongy mass filling the ventricle below. The soft, thick tissue thins out and becomes the curtain of the auriculo-ventricular valve, and at its free margin retains its connection with the muscular and fibrous tissue in the ventricle. The latter becomes differentiated into the papillary muscles and the normal chordæ tendinæ. The chordæ change from muscular to fibrous tissue at about the fifth month[13]. As the spongy mass of the trabeculæ becomes invested with the endocardium and retreats toward the compact muscular wall it may happen that occasionally some band or bands of the reticulated structure are left stretched across the cavity. The condition is somewhat analogous to that in the heart of the serpent, where the trabeculæ exist all over the surface of both ventricles and even form the imperfect cribriform septum[2]. Some of the aberrant cords are seen by the naked eye to be largely muscular, and the microscope has discovered muscle-fibers in many others, so that there is little doubt of their origin from muscular tissue[14]. Such thin muscular cords removed from vascular connection with the rest of the heart-muscle, and stretched in the cavity, may easily atrophy and become fibrous. The reticulated masses observed by Chiari in the right auri-

cle can, I think, be explained similarly as overgrown trabeculæ which have lost their muscular character and become fibrous. The aberrant cords of the third class which were seen by Feigl[7] and Browicz[5] to run from the valve of the foramen ovale to be attached to the free margin of the atrio-ventricular valve, I think, can be explained as being merely exaggerations of those overgrowths of the valve of the foramen ovale observed by Turner[15] and Fowler[9]. The development of the foramen ovale in man is still somewhat in dispute between the followers of His and of Born. His thought that the atrial septum arose from a sickle-shaped process growing from above and behind, and another growing from in front and below, leaving between them the foramen ovale, the former process forming the limbus of Vieussens and the latter the valve of the foramen ovale. Born, studying the hearts of rabbits, thought that the atrial septum grew entirely from behind and above, and that the foramen ovale arose as a new opening, just before the atrial septum united with the septum ventriculorum below. The foramen ovale became closed after birth by the limbus of Vieussens, which had grown down from above and behind as an independent sickle-shaped process of the auricular wall. The appearance in the adult, in whom the valve of the foramen ovale is a distinct valve, would, in my mind, point to the truth of His' theory. Also the occurrence of the anomalies described by Fowler and Turner are best explained on the former hypothesis. The folding in of the valve from the atrio-ventricular septum below might cause also irregular foldings of the endocardium in the neighborhood of the atrio-ventricular valves and the production of the anomalous bands running from the edge of the valve of the foramen ovale along the floor of the auricle towards the mitral curtains, and even extending upon them, as in the exaggerated examples reported by Feigl and Browicz. There is, however, still so much that is vague

in the embryology of the septa and the valves of the heart that further investigation is needed before the final word is said.

It is obvious that the only variety of aberrant tendinous cord which can have clinical significance is the second, viz., the cord extending across the cavity of the chamber, unless indeed those of the third class might possibly interfere with the full opening of the mitral valve. The only reported cases are the former. The apparent cause of the clinical signs which may be observed when a diagnosis is made during life is the vibrating of the tense thread by the action of the blood-stream. The cords so diagnosticated have almost always been in the left ventricle and stretched across its upper part. In this situation only could the blood-current between aorta and ventricle act upon them so as to cause enough vibration to give forth the characteristic murmur. This murmur is a high-pitched musical note exactly resembling the twanging of a bow or fiddle-string. Huchard expressed the conceit that the blood-current plays the role of the archer in vibrating the bowstring. In most of the cases recorded the murmur is heard best at the base of the heart or over the xiphoid. The propagation of the sound is usually upward toward the neck. It is usually systolic in time. In a case of Reynaud's, however[16], the musical sound due to the cord accompanied the diastolic soufflé of a coexistent aortic insufficiency. Probably in this case the tightened string was set in vibration by the recurrent stream through the regurgitant aortic valve. The section showed a cord running across the upper part of the left ventricle from the anterior columna carnea to the ventricular septum, thus lying directly in the way of the returning blood from the aorta.

At a meeting of the New York Pathological Society held in 1892, three cases were reported of chordæ tendineæ across the cavity of the left ventricle, wherein dur-

ing life musical murmurs had been heard at the base transmitted into the vessels of the neck, and in one also a diastolic murmur heard only at the base[4]. Huchard[3] reports three cases confirmed by autopsy after ante-mortem diagnosis from physical signs. These signs were musical systolic murmurs and vibratory thrills. In one of the cases there was coagulation about the cord. Huchard says these cords are usually congenital, but may rarely be due to sclerous atrophy of the muscular trabeculæ and they always occur in the left ventricle. In the last statement he is clearly in error, for others besides myself have observed such bands in the right ventricle, and, as before stated, in the left auricle. Sir William Turner[15] mentions two hearts with fibrous cords—moderator bands, he calls them—in the left ventricle, and in one of these cases there was also a fleshy moderator band in the right ventricle.

In most of the cases in which an ante-mortem diagnosis was made, there coexisted some valvular lesion, with more or less marked hypertrophy and dilatation of the left ventricle. There is often a distinct vibratory thrill to be felt over the region where the musical murmur is best heard. Whether this thrill is due to the vibrating of the cord, or to the condition of dilatation itself is, perhaps, questionable. That the cardiac hypertrophy is essential to the presence of the musical murmur is evidenced by one case of Huchard's[17] in which the hypertrophy existed with the musical murmur, although the sound diminished and finally disappeared *pari passu* with the advance of asthenia of the heart.

Hamerujk[18], in 1843, first observed that musical heart-murmurs might arise solely from the chordæ tendineæ. Before that time general opinion had agreed with Lænnec, who said such sounds were heard only in the vessels and never in the heart. The musical murmur caused by aberrant cords can not be said to differ much from the musical murmur heard in some cases of aortic

stenosis, osseous or calcareous concretions on the valve, or by rudimentary supernumerary valves[19]. Mayne[20] reports a case in which there was a loud, high-pitched musical sound heard ever at some distance from the chest. This was systolic and most intense at the apex. The man was free from signs of other cardiac anomaly until five or six years later, when he came under observation for marked symptoms of aortic stenosis. The autopsy, two years afterwards, showed a much narrowed aortic orifice and two cords crossing the left ventricular cavity, just below the aortic entrance. These were, doubtless, set in vibration by the direct stream from ventricle to aorta, and consequently, the characteristic musical bruit was heard with systole. A similar case was reported in 1879 by Verardini[23]. In a case of Engel's[21] the murmur was prediastolic, and was probably caused by the regurgitant stream through an insufficient aorta. There was in this case a fine string of fibrous tissue across the aortic orifice and attached at one end to a pocket of the aortic valve. Schroetter[22] thinks that such a cord might arise in consequence of endocarditis, where one end of a normal tendinous cord might become torn away and be attached again by its free end in an abnormal situation.

Potain[24], in 1876, observed a case of mitral insufficiency, with its characteristic systolic murmur at the apex, and, in addition, a musical murmur at the base. A cord ran from the anterior mitral curtain to the ventricular wall, just below the aortic orifice. Demange[25] in an admirable article on the causes of musical heart-sounds, records a similar condition of things in the right ventricle. A woman of 70 had chronic emphysema and other conditions, giving rise to a dilatation of the cavities of the heart and a consequent relative insufficiency of the tricuspid, causing a slight systolic soufflé at the point of the sternum. Also, toward the base of the sternum there was a loud musical twang heard with the

systole. The autopsy revealed, among other conditions, a tendinous cord across the right ventricle running in front of the tricuspid valve and attached to the opposite walls. This is the only case I have found in which clinical signs were given by a cord in any other cavity than the left ventricle.

Besides adding murmurs to obscure the cardiac sounds, these aberrant tendinous cords of the second class may have other clinical significance. They may serve as points on which the blood may clot[17] or possibly might interfere with the complete opening or closing of the mitral or tricuspid valve. They might rupture when diseased in the same way that the normal cords of the mitral valve sometimes do. Indeed the cords may sometimes have a beneficial influence in preventing undue dilatation of the ventricle.[15,2].

In recapitulation we may remember that the aberrant tendinous cords of the heart may be divided into three main classes: First, those running longitudinally along the wall; second, those running across the chamber, and, in some cases in which they are situated in the upper part of the ventricle, giving rise to definite clinical symptoms; and, third, that rare class extending from auricle to ventricle and not, as far as observed, giving rise to ante-mortem signs. Since some of the hearts which I dissected were preserved for dissection solely because of their aberrant cords, I have no right to make deductions as to frequency, but I think that it will be admitted that these cords will be found oftener than is generally supposed if carefully looked for in an unmutilated heart. They are usually congenital, although in some cases it seems probable that they may arise from sclerous degeneration of a muscular band or trabecula, along with a general fibrosis of the cardiac muscle. Possibly some few may arise from rupture of a normal cord and reimplantation of the free end. The characteristic murmurs usually occur in hearts hypertrophied and

dilated from coexisting valvular disease, and only then when the cord is stretched in the course of the direct or regurgitant blood current which sets the strain in vibration.

March 14, 1898.

BIBLIOGRAPHY.

1. Quain's Anatomy, 9th ed., vol. ii. p. 846.
2. Macdonald Brown: Jour Anat. and Phys., 1889, p. 250.
3. Huchard: Bull. et Mém. de la Soc. méd., des Hôp., Paris, No. 9, 1892.
4. Stearns and Byron: Epitome of Medicine, N. Y., Sept., 1892.
5. Browicz: Virchow's Archiv, Bd. 145, Heft 3, 1896.
6. Bisiadecki: Untersuch. aus dem Path. Inst. Krakow, 1871.
7. Feigl: Verh. des 11. Cong. poln. Aerzte und Chir., Lemberg, 1875.
8. Chiari: Beiträge zur path. Anat. u zur allg. Path., Bd. xxi.
9. J. K. Fowler: Trans. London Path. Soc., 1882, p. 77.
10. Rolleston: Proc. Anat. Soc. Gr. Brit. and Ire., 1896, p. v.
11. W. Griffith: Ibid., p. vi.
12. Schaeffer: Quain's Anat., vol. i pt. i 10th ed., p. 145.
13. Minot: Human Embryology, p. 534.
14. Oehl: Mem. della acad. delle scienze, Torino, vol. 20.
15. Sir Wm. Turner: Jour Anat. and Phys., 1895-6, p. 568.
16. Surbled: Thèse de Paris, 1879.
17. Huchard: Rev. de méd., Paris, 1893, p. 113.
18. Hamerujk: Med. Jahrb, Wien, Bd. xlix, 1843.
19. Banks: Dublin Hospital Gazette, (see 20).
20. Mayne: Dublin, J. M. S., 1870, p. 496.
21. Hugo Engel: Philadelphia Med. Times, March 8, 1884, p. 415.
22. Schroetter: Wiener med. Blätt., No. 1, 1883 (see 21).
23. F. Veradini: Bull. delle Sc. med. Bologna, 1879, p. 305.
24. Potain: Bull. Soc. Anat. 1876. p. 244.
25. E. Demange: Bull. Soc. de méd. de Nancy, 1878-80, p. 21.
26. S. West: Tr. London Path. Soc., 1882, p. 75.

FENESTRATION OF THE PULMONARY VALVES: RUDIMENTARY FOURTH VALVE TO SUPPLY THE DEFECT.

T. R. CROWDER.

This heart was removed from a man 32 years of age, who died in the Presbyterian Hospital, February 28. He had an acute nephritis, complicated by pleuritis with effusion and compression of the lung. The body was well developed, symmetrical and well nourished. So far as could be ascertained there had never been symptoms referable to disease or impaired function of the heart. During his last illness there were no physical signs of any cardiac lesion.

The heart is of about normal size. The epicardium shows no changes. The aortic and pulmonary valves were competent to water. The right ventricle contained a small amount of clotted blood; the left was empty. The entire endocardium is smooth. The mitral and tricuspid valves are negative. One of the aortic cusps shows a slit-like fenestrum lying parallel to its free margin; they are otherwise negative.

There are four pulmonary cusps instead of the normal three. Three of these are of equal size and situated normally. The fourth is of about half the width of each of the other three. It is situated between the adjacent attached margins of the anterior and the right posterior cusps and lies on the same level on its ventricular side. The two cusps lying on either side of this supernumerary valve show in the adjacent half of each large fenestra. In the posterior one is a single large triangular opening with its base toward the center of the valve and its apex at the angle. This opening occupies about one-third of the right half of the valve. A long slit-like opening lies parallel and close to the free margin of the opposite half. The right half of the anterior valve shows an opening corresponding in outline and size to that in the right posterior and lies exactly opposite to it. The large opening is divided into five smaller ones by fine fibrous strands; and surrounding it are several smaller slit-like fenestra. When the valves are brought together, as in the normal closure, it is seen that the rudimentary fourth largely closes in the defects in the other two. It is not so long from its attached base to the free margin, thus it lies on a lower level in closure than the others and its free margin fits quite accurately to the sides of the triangular openings lying closest to the bases of the valves. The margin of this fourth valve is held more accurately in place by two long, thin, cylindrical, fibrous strands stretching from near its center to the angles of attachment of the two adjacent valves.

March 13, 1899.

PRIMARY DIFFUSE SMALL CELLED SARCOMA OF THE PARIETAL PERICARDIUM.

J. C. WILLIAMS AND A. L. MILLER.

Malignant growths of the pericardium are very rare. A study of the available literature upon this subject simply emphasizes this fact. Bauer[1] in his article on the pericardium in Ziemssen's Encyclopedia says: "Carcinoma very rarely occurs in the pericardial sac, and when it does, it is as an extension of the disease from neighboring parts, particularly from the mediastinum, sternum or esophagus on to the pericardium.

"Much more rarely do we find nodules on the pericardium secondary to acute miliary carcinoma in other serous membranes.

"Kohler found cancer of the pericardium six times in 9118 autopsies; Günsberg one in 1700; and Willigk, in 477 autopsies on patients dying of cancer, found the pericardium affected seven times.

"When the new growth extends to the pericardium from neighboring parts, the parietal layer shows, as a rule, a diffuse infiltration of cancer, or else the mass grows from a single limited spot and projects in nodules into the sac. Associated with it, there is almost always a fluid effusion into the cavity. The fluid is frequently hemorrhagic in character, sometimes purulent and ichorous, and again in other cases it has more the appearance of serum, etc."

In the above extract carcinoma only is spoken of, but, as sarcoma is not mentioned at all in connection with the pericardium, it may be inferred that all malignant growths of this structure are included under the one term carcinoma.

Whittaker[2], in the Twentieth Century Practice of Medicine, includes the whole subject of malignant growths of the pericardium under the one heading "can-

cer," and says: "The pericardium is an infrequent site of malignant disease. Such deposits are usually metastatic. Primary deposits imply affection of the lymph glands of the pericardium, etc."

In the available literature upon the subject the writer has found recorded the following cases:

Haldane[3] in 1854 reported a case of "cancer of the pericardium" in which small cancerous deposits were found upon the surface of the left ventricle near the base of the heart together with some involvement of the parietal layer of the pericardium. Nodules were also found in the liver, lungs, spleen and kidneys.

Kaulich[4] in 1862 reported a case of "carcinoma of the pericardium under the symptom of pericardial exudate," in which both layers of the pericardium were involved in a dense nodular growth.

Church[5] in 1868 reported a case of "carcinoma of the pericardium, anterior mediastinum and the lymphatic glands of the thorax and abdomen," in which the parietal layer of the pericardium was enormously thickened by a diffuse growth, the visceral layer having but a few nodules scattered over it.

Nichols[6] in 1869 reported a case of "malignant disease of the pericardium simulating aortic aneurysm," in which the parietal layer of the pericardium was very greatly thickened, being about three inches in thickness over the base of the heart, and varying from that to a very slight thickening over the diaphragm. The visceral layer was not involved.

Clay[7] in 1869 reported a case of "fibro-nucleated or cancroid growth in the pericardium," in which the parietal layer of the pericardium was very greatly thickened, being about two inches thick over the base of the heart, and varying from that to about one-eighth of an inch over the diaphragm. The visceral layer was not involved.

Broadbent[8] in 1882 reported a case of "malignant

disease (sarcoma) of the pericardium," in which the parietal layer of the pericardium was very much thickened, being about one and one-half inches in thickness over the base of the heart, and varying from that to about one-third of an inch over the diaphragm. The visceral layer was quite normal.

Guarnieri[9] in 1886 reported a case of "primary endothelial cancer of the pericardium" (Un caso di cancro endotheliale primitivo del pericardio) in which the visceral layer of the pericardium was almost entirely covered with small greyish-white nodules varying in size from that of a grain of millet to half a pea.

The structure in this case was alveolar, the walls of the alveoli being made up of a rather delicate connective tissue, the alveolar spaces being filled with comparatively large rounded or oval cells containing large vesicular nuclei.

Hektoen[10] in 1893 reported a probable case of primary round-celled sarcoma of the pericardium in which the neoplasm was found upon the anterior surface of the heart near the base and was made up of a mass of small round cells and fibrous stroma.

Whittaker, in his article referred to above, mentions a case of "primary endothelioma in the lymphatics of the pericardium reported by Marchiafava, a case of sarcoma of the pericardium and bronchial glands reported by Liborius, and two cases of 'primary cancer of the pericardium' cited by Bernheim as being reported by Foerster and Le Beuf."

References to these articles are not given in the "Index Catalogue" of the library of the surgeon-general's office at Washington, excepting the one by Le Beuf, which was reported in 1886; the writer has been unable to consult the original articles in which these cases are described.

The case I would add to this list is one which occurred in the practice of Dr. A. L. Miller of Dixon, Ill., who

furnished the clinical history, and made the post-mortem examination. The specimen and photographs of the neoplasm were sent to Professor Hektoen of Rush Medical College. The writer is personally indebted to Professor Hektoen for the privilege of reporting the case. The clinical and post-mortem reports as supplied by Dr. Miller, are as follows:

The patient, Eddie B., a boy about 13 years of age, was brought to my office Dec. 29, 1896. Family history as follows:

Parents living and well. Of the two children born to them, the other, a girl, died at the age of 2 years and 6 months after a two days' illness. Maternal grandmother died at the age of 42 of dyspepsia (?) after an illness of four years' duration. Maternal grandfather died at the age of 70 of carcinoma of the stomach, revealed by post-mortem. Paternal grandfather died at the age of 75 of carcinoma of the stomach, revealed by post-mortem. One aunt died of carcinoma of the breast.

Personal History.—The boy had never had any illness except in October, 1895, when the writer attended him through an attack of tonsillitis. He was of spare build, nervous temperment, weighing 64 pounds. In May, 1896, he began to complain of being tired and hungry; he was always tired and hungry. In September, 1896, his parents first noticed that he had choking spells in his sleep, at which times his limbs would twitch and jerk.

When first seen he was very pale and emaciated. There was dulness on percussion over all of the left lung except a small area posteriorly. Auscultation gave a clear respiratory murmur over a space about two inches in diameter posteriorly, and absence of respiratory sounds elsewhere. The right lung was normal. He had a short, harsh, unproductive cough.

Respiration was 30, pulse 120, and very weak, rhythm irregular. No cardiac murmurs. The apex beat was seen one inch to the left of the ensiform cartilage. The force of the beat was much increased, the impulse could be plainly seen at a distance of twenty feet. At this time the temperature was normal. About two weeks after the first examination he was taken with pain in the left chest, which was followed by an effusion into the pleural cavity, the intercostal spaces bulging.

The temperature was 102° F. at this time. The intercostal bulging disappeared in about five days, but the bulging of the entire left chest wall was progressive from this time on.

For several days a loud spashing noise could be heard at a distance of three or four feet. It seemed to be synchronous with the heart beat.

There was considerable pain at times but not during the last five weeks of life. During this latter period the apex impulse

could not be detected. From the first there was a marked depression just below the ribs in the nipple line and extending backwards. This depression gradually filled in and became bulging during the last few weeks, at which time the hard tumor could be readily felt by pressing the fingers up under the ribs. The appetite was good to the last, but deglutition was very difficult. Hot food gave much distress. Dyspnea was marked and progressive. The last few weeks he could breathe only in one position, that is, leaning forward at an angle of about 45 degrees and to the left with his head resting upon a low table.

General dropsy developed during the last few weeks, his cheeks, owing to his position, hung down like great water sacks.

He died April 2, 1897, having been under observation three months. Dr. J. B. Snyder of Polo, Ill., saw him in consultation and was present at the post-mortem examination. The post-mortem findings were as follows:

The left chest bulged forward an inch and a half more than the right. Examination showed a large tumor developed uniformly over the pericardium and adherent to the chest walls anteriorly and to the diaphragm below. The left lung was solidly compressed and there was almost no room left for expansion of the right lung, the tumor filling almost the whole of the chest cavity. No glandular enlargements were found.

The weight of the tumor with the lungs attached was 6¼ pounds. On incising the growth the heart was found free in the pericardial cavity.

Macroscopic appearance of the growth.—The neoplasm is a large, irregularly rounded, lobulated mass of a yellowish white color, of a fairly hard consistency, but it tears apart very easily. The anterior surface is rather flat and has the appearance of having been firmly attached to the under surface of the sternum and costal cartilages. The under surface is firmly attached to and involves the diaphragm. The sides show a distinctly lobulated appearance, the right side especially showing several large lobes separated by deep fissures, the free surface of the lobes being quite smooth.

The upper surface is rather irregular in outline and shows in front the remains of adhesions and the cut ends of the innominate artery, the left common carotid and the left subclavian arteries, the innominate veins and just back of these is the cut end of the esophagus

on either side of which are smooth tumor areas, still farther out and posteriorly are seen the apices of both lungs which are separate from the neoplasm at this point, but show some white areas in their substance indicating the invasion of the lung tissue by the growth. The posterior surface may, for convenience of description, be divided into three zones, a left, a middle and a right.

The left zone shows above and to the outer side the posterior surface of the upper lobe of the left lung, the upper two-thirds of which looks normal with the exception of small whitish areas scattered here and there, the lower third is changed to a firm whitish mass. To the inner side and below is seen the inner upper part of the fissure filled with a firm white mass of tumor tissue. The inner upper portion of the lower lobe is fairly free from the growth, but the lower portion is involved in quite a large mass of tumor tissue.

The middle zone, the space between the lungs, shows two ridges of tumor tissue extending from above downward and separated by a furrow or depression in the depths of which are seen the esophagus and the descending aorta which are nearly surrounded by but are not involved in the growth; no enlarged glands can be seen in this area.

The right zone shows practically nothing but the posterior surface of the right lung which looks nearly normal with the exception of the inner portion of the principal fissure where some small areas of tumor tissue can be seen.

The dimensions of the growth are as follows:

The vertical antero-posterior circumference, 48 cm. the transverse circumference at its widest portion, including both lungs, 44 cm. The weight of the neoplasm with heart and lungs, is 6¼ pounds.

On incising the neoplasm from above downward in the median line in front there was disclosed to view a

cavity, and lying within this cavity was the heart free and practically normal in appearance.

The cavity is lined by a membrane which is somewhat nodulated, none of the nodules being larger than half a pea, and has lost the smooth glistening appearance of the normal pericardium excepting in a small triangular area just posterior to the heart where the appearance is quite normal. The pericardial cavity measures from above downward, 11 cm., from side to side at the widest part, 11 cm., from before backward at the widest part above, 4 cm.

The heart appears quite normal, slightly smaller perhaps than it should be, covered by an apparently normal pericardial membrane.

The coronary arteries are normal. Near the beginning of the aorta at its left anterior side is a patch about 1 cm. by 3 cm. in size, where the heart wall had apparently become adherent to the parietal pericardium. The endocardium presented nothing abnormal. The thickening of the pericardium in this case is quite enormous, varying from 6½ cm. in front just opposite the base of the heart to about 1 cm. over the diaphragm.

At the bottom of one of the fissures on the right side, near the root of the lung, is an area in which the pericardial membrane is thickened very little if any.

Dissection at the root of both lungs shows the peribronchial lymph glands to be somewhat enlarged, but not greatly, the largest one found being not larger than a lima bean.

Microscopic findings.—The neoplasm, as revealed by sections taken from different portions of it, is composed of a mass of cells and a very scanty amount of fibroelastic intercellular substance. The cells which make up almost the whole of the growth, are massed together with no regularity of arrangement. They are small, round, comparatively uniform in size and contain nuclei which nearly fill the cell body. A study of these

nuclei reveals a difference in reaction to stain which is probably due to a difference in the stage of the development of the cell.

There seem to be two distinct types of cell with apparently several grades between. One type contains a smaller, round nucleus taking a deep uniform stain. The other type contains a nucleus which is slightly larger, irregularly oval in shape, takes a faint stain and is quite granular in structure. Between these two extremes are cells, some resembling one type and some the other, and look like cells that are in the transition stage. The intercellular substance is fibro-elastic in structure, containing a very few elongated thread-like nuclei. The amount varies greatly in different portions of the neoplasm. On the whole it is very scanty. Here and there are heavy dashes of this structure looking like narrow bands running through the neoplasm, and from these bands can be seen, in places, the fine fibrillar processes running out and forming the fine meshwork which supports the tumor cells.

The blood-vessels are very small, not numerous, and the great majority of them have distinct endothelial walls. The pericardial surface of the growth shows a layer about 1 mm. in thickness, which differs from the remainder of the growth in that there is a far greater amount of the fibro-elastic structure present, the fibers of which run parallel with the free surface. In between the fibers are rows and groups of the round tumor cells, running parallel with and infiltrating out to the free surface. The normal endothelium of the pericardium can not be made out.

A section through the wall of the left ventricle shows no marked change in the myocardium, the epicardium being also practically normal, except in its lower lymphatic layer where here and there a few small round cells are seen.

The endocardium shows no change in structure.

A section through the wall of the aorta just above the valves shows the aortic wall to be practically unchanged, but surrounded by tumor tissue; the same holds true of the wall of the pulmonary artery.

A section through the wall of the right bronchus near the root of the lung shows the entire wall, except the plates of cartilage, to be invaded by the round cell growth; in fact, the wall is almost entirely made up of tumor tissue; here and there on the inner surface can be seen some of the normal columnar ciliated epithelium still remaining and also underneath this a few of the mucous glands imbedded in the tumor tissue; sections through several of the slightly enlarged peribronchial lymph glands show the gland outline to be fairly well preserved, the capsule still showing as a very thin but traceable layer of connective tissue. Within this capsule the structure is almost identical with that of the primary neoplasm; here and there near the periphery are a few small round areas of denser aggregations of round cells but all resemblance to the normal structure and arrangement of the lymph gland is lost.

A section through the diaphragm shows a layer of tumor tissue upon its upper pericardial surface. Passing down to the musculature of the diaphragm we find the small tumor cell invading the muscle tissue, passing in between the bundles of fibers and infiltrating in among the individual fibers themselves, compressing them and in some places entirely replacing them.

The growth passes through the musculature and forms a distinct layer upon the peritoneal side. A study of the peritoneum at this point reveals its endothelium to be intact.

Remarks.—As to the nature of this neoplasm there can be no doubt that it is a small round-celled sarcoma. The question of greatest interest is where did it originate? Unfortunately in this case it is impossible to determine accurately the exact point of origin.

In view of the following facts: 1. The enormous uniform thickening of the pericardium. 2. The freedom of the pericardium from invasion. 3. The very slight enlargement of the peribronchial and mediastinal glands. 4. The statement in the post-mortem report that "no glandular enlargements were found elsewhere; it seems to the writer reasonable and fair to assume at least the very great probability of its having originated in the pericardium itself in its lymphatic layer. A review of these reported cases reveals two distinct types of involvement of the pericardium by these growths, one occurring as a diffuse, uniform and often enormous thickening of the parietal layer, and the other occcurring as a discrete, nodular growth upon the visceral portion.

It is of a great deal of clinical interest in regard to these obscure and rare cases to note that in every one of the reported instances where a clinical history was obtainable one of the earliest and most pronounced symptoms was dyspneic attacks, severe and urgent, which would continue with greater or less severity and urgency throughout the course of the disease.

February 13, 1899.

BIBLIOGRAPHY.

1. Ziemssen's Encyclopedia, 1881, vol. vi, p. 626.
2. Twentieth Century Practice of Medicine, 1895, vol. iv, p. 8.
3. Monthly Journal Med. Society of London and Edinb., 1851, vol. xix, p. 77.
4. Vrtljschr. f. d. prakt. Heilk., Prag., 1862, vol. lxxiii, p. 78.
5. Trans. Path. Soc. of London, 1868-69, vol. xix. p. 64.
6. St. George's Hospital Reports, London, 1869, vol. iv, p. 221.
7. Edinb. Med. Jour., 1869-70, vol. xv, pp. 802-804.
8. Trans. Path Soc. of London, 1881-82, vol. xxxiii, pp. 78-81.
9. Arch. per le Sc. Med., Torino, 1886-87, vol. ii.
10. Medical News, Nov. 18, 1893.

INFECTION WITH THE STREPTOCOCCUS PYOGENES.

REPORT OF A CASE IN WHICH THERE OCCURRED A STENOSIS OF THE PULMONARY CONUS, AN ANEURYSM OF THE RIGHT VENTRICULAR WALL, HEALED AND MORE RECENT METASTATIC ABSCESSES IN THE LUNGS AND FOCAL NECROSES IN THE RENAL GLOMERULI.

A. C. COTTON AND E. R. LE COUNT.

Clinical History: *Abstract.*—E. L., male, age 11 years 9 months. At the age of four months, according to the statement of his mother, he had pneumonia, and this was followed by diphtheria, mumps, measles, whooping-cough, typhoid fever and scarlatina. He was continuously ill until three and one-half years of age; he walked at 4. This was followed by two years of health; he then had an attack of severe and obstinate expistaxis, for which plugging of the nostrils was necessary. Epistaxis recurred frequently. He first came under observation Aug. 2, 1898, and for two months had suffered from dyspnea and gradual loss of strength.

Examination showed the following: Emaciation; pallor of skin and mucous membrane; skin dry and scaling; petechia on the legs; tips of fingers slightly clubbed; edema of face and feet; tongue coated; diminished resonance over the apex of the right lung; a marked systolic thrill over the apex of the heart; pulsation of the lower part of the sternum and epigastrium; the systolic thrill felt in greatest intensity in second left interspace; right border of cardiac dulness is two fingers breadth beyond right border of the sternum; a harsh systolic murmur heard all over the chest, loudest in the second left interspace at which point the second sound of the heart is not distinguishable; epigastric region bulging; liver extends the breadth of three fingers below the costal arch; spleen palpable.

For the following two weeks he had constantly a temperature slightly above the normal and developed a harsh dry cough.

August 19: Temperature 104.5, pulse 110, respirations 38; fine râles over both lungs.

August 23: Temperature 104.6; friction sounds over the right lung.

The sputum was examined during September and October for tubercle bacilli: result negative.

Examination of the blood September 7 showed hemoglobin 40 per cent.; red blood corpuscles 2,640,000, white blood corpuscles 12,300.

October 1, albumen appeared in the urine and it increased

in amount daily. October 5, two molars were extracted for alveolar abscesses, and there occurred a suppuration of the alveolar process on the left side of the upper jaw which extended so that by October 19 it reached nearly to the median line and backward to the soft palate. The left side of the face became greatly swollen and the left eye closed; the breath was foul. On October 21 the suppurative and gangrenous inflammation had extended across the median line and pus was discharged from the left nostril and left auditory meatus. The neck was edematous and the cervical glands enlarged. On the following day suppuration was manifest in the left orbital cavity. Death took place on the 24th.

The clinical diagnosis was infective endocarditis.

Necropsy: Anatomic Diagnosis.—Stenosis of the pulmonary conus; malformation of the pulmonary valve (2 cusps); aneurism of the right ventrical wall; acute mural endocarditis; defective (perforate) ventricular septum; fibrinous pleuritis; old healed and recent metastatic abscesses of both lungs; cloudy swelling of the liver and kidneys; chronic splenitis; acute perisplenitis; general anemia; anasarca, hydrothorax, hydropericardium and ascites; panophthalmitis of the left eye.

The body is very pale, with a greenish discoloration of the lower part of the abdomen. A puncture (post-mortem) wound is present one inch to the left of the navel. The palms of the hands are edematous. The lids of the left eye are matted together by a sticky secretion, and there is a marked exophthalamos of this eye. The subcutaneous fat exposed by the median incision is scanty and edematous. The diaphragm extends upward on the right side to the fifth rib, and on the left side to the fifth interspace. The bladder is distended with clear urine. The peritoneal cavity contains a considerable quantity (from two to three pints) of a clear fluid. Adhesions which are easily broken occur about the spleen. The pleural cavities are each about one-half filled with a clear fluid. The gall-bladder is distended with thick dark bile; its mucous membrane is edematous, and its cavity is uninterrupted. The sigmoid flexure reaches as a distended coil upward and to the right, to a point opposite the navel. The ureter on the right side is dilated to the size of a lead-pencil, the walls being thin. The back of the tongue is of a grayish black color. The tonsils are both atrophic and pigmented, being of a slaty blue color. The musculature of the tongue is dry and pale. The esophageal mucosa is yellowish and smooth. The larynx and trachea possess linings covered with a frothy, greenish mucus. The pericardial cavity contains a quantity of clear, opalescent fluid.

The heart measures 10 c.m. across the base, 9.5 c.m. from the base to the apex, and 5 c.m. in thickness. It weighs 170 g. Both the mitral and tricuspid valves admit three finger

tips. The aortic and pulmonary valves appear competent to the water test. The mitral cusps exhibit no changes. The posterior cusp of the tricuspid valve is thickened along its free margin. There are no changes about the aortic valves, except that all three cusps show slight fenestration of the margins. Below the aortic valves, in front and above the interventricular septum, is a pouch which easily contains the bulbous tip of a finger, and is from twelve to fourteen millimeters in diameter. At the bottom of this pouch is a small hole, two millimeters in diameter, through which a probe can be passed into the right ventricle, where it emerges just below the stenosis in the conus, and just below the tricuspid valve. This pouch lies in the "unprotected space." The endocardium on the septum below the pouch (left ventricle) is thickened and of a whitish color. The left ventricle measures 6.5 c.m. long; the wall averages 12 m.m. The right ventricle shows near its upper left-hand corner, just below the pulmonary valve, a stenosis of the conus. The opening measures 9 m.m. in diameter and approximately 2.5 c.m. in circumference. This stenosis is 14 m.m. below the pulmonary cusps, of which there are but two. Below these cusps and between the pulmonary valves and the point of stenosis in the conus, is a cavity extending outward in the heart wall. It extends for a distance of 3.5 to 3.8 c.m. forward and to the right in the wall of the right ventricle. With the heart unopened it lies in front of the large vessels. Its walls are thin, covered with a whitish, smooth lining. It is crossed by numerous bands of myocardium which resemble the trabeculæ of the ventricular walls. Among these trabeculæ is a quantity of whitish and yellowish gray, clotted blood, somewhat adherent in places, and which in some spots leaves a rough surface when it is removed. The wall of this aneurismal sac at its thinnest point measures 2 m.m. The right ventricle measures 6.5 c.m. in length and averages from 12 to 14 m.m. in thickness. The foramen ovale is closed. The right auricle is dilated and its walls appear thickened. No signs of a ductus Botalli were found, nor any changes in the pericardium nor in the coronary vessels.

Left Lung.—Over the lower lobe is a delicate, fibrinous exudate. At the margin of this lobe, below and laterally is an area of consolidation, which on section shows a cavity filled with grayish-yellow pus. There are also areas of consolidation, minute and buckshot sized, which contain a dry, yellowish, granular material. There are no changes in the surrounding lung tissue, aside from a wall formation. At the upper part of this lobe, there is an area of consolidation somewhat wedge-shaped, and reddish on section, which shows at the bottom a thrombosed vessel. The thrombus is occluding and grayish yellow in color, and is adherent. In the apex of this lung is an old cavity, the size of a walnut, containing gas or air, which

collapses on pressure. It is provided with a definite, fibrinous wall, a somewhat trabeculated cavity; there are no changes in the surrounding lung tissue. Also in the upper lobe, there are some nodules, similar to those in the lower lobe.

The right lung possesses a fibrinous exudate externally, similar to that on the left lung. In the lower border of the right lower lobe is an old cavity with smooth walls. It is empty. There are no changes in the surrounding lung tissue. The middle lobe shows no changes. The upper lobe, in the apex possesses a cavity, similar to, but smaller than that in the left upper lobe. Deeper in the right upper lobe is a similar, but larger cavity. Both lungs float, both are pinkish in color and crepitation is fair. The glands at the roots of the lungs are enlarged, and dark red in color; they show no caseous areas, and only slight blackening by coal pigment.

The liver measures 21.5x15x11x5 c.m. and weighs 950 g. On section it presents a mottled appearance, with rather gross, yellowish areas. It is soft and the lobular markings are distinct.

The spleen is 15.8 c. m. long and 8 c.m. wide, and 4.5 c.m. thick. There are fibrous tags on the capsule. On section it is soft. The malphigian bodies, which are very numerous, are large and whitish in appearance. Weight 290 g.

The kidneys are equal in size, weighing together 315 g. and measuring 11.5x6.5x4.5 c.m. The left kidney is practically bloodless. The fat of the pelves is edematous. The capsules are easily removed. The cortex of the left kidney is pale and of a glossy appearance. The cortical markings are quite distinct. The glomeruli project as pale bodies.

The bladder has a pale mucosa; a fibrous nodule, 12 m.m. long, occurs at its apex. It is firm and whitish on section. No changes are presented about the prostate gland, nor the seminal vesicles.

The intestines, pancreas and other viscera show no gross changes. Examination of the brain and the left eye was not allowed.

ABSTRACT.

Microscopic Examination.—The interesting changes center in the lungs and kidneys. One of the small areas of consolidation from the left lung has undergone a marked necrosis in which all signs of alveolation have disappeared. This necrosis is irregular in outline and appears to have taken place in patches which have fused. In this necrotic tissue are medium sized blood-vessels which are completely filled with thrombi. The lung tissue around is consolidated by fibrillated cells and leucocytes which fill the alvecli. The firm fibrous walls of these cavities were examined and all showed essentially the same features. The wall is made up of fibrous tissue which stains mainly with eosin, the cells in the wall are fibrillated and

possess undulating ends: there are also some cells with oval nuclei and some granules of blood pigment. The alveoli in the immediate vicinity are quite crowded with small oval or round cells and red blood corpuscles. The spleen shows a superficial necrosis which includes the capsule and a narrow zone just beneath it. In this necrotic tissue there is considerable fibrin. The spleen corpuscules contain a large number of red blood cells, and in a few cells of the corpuscles proper the nuclear staining is deficient. In the kidney very striking changes are present in the glomeruli; the nuclei present far exceed the normal in number, most of them are small and oval, and it is difficult to outline the cell bodies; almost without exception the glomeruli contain numerous cells which are very much fibrillated and drawn out into narrow necked projections. In addition to these features many glomeruli contain areas which are reddish from the eosin staining, and in such areas the nuclei are few and extremely distorted, such eosin staining areas occupy but a small portion of the glomerulus and are usually at the periphery, they are crescent shaped and sometimes so closely fused to Bowman's capsule that it is difficult to say whether they are due to changes which have taken place in a mass of cells which accumulated between the glomerulus and its capsule or to changes in a portion of the glomerulus itself. Weigert's fibrin stain does not reveal any fibrin in these areas nor can bacteria be found by Gram's staining or other methods. Sections of the thyroid, adrenals, intestines, pancreas and heart muscle show no important changes. The liver contains "lymphoid nodules;" the nuclei of the liver cells do not react uniformly to nuclear dyes, some staining much more darkly than others. A great variety of leucocytes (?) are present in the capillaries—for the main part mono-nuclear, and exhibiting the changes of nuclear death.

Bacteriologic Examination.—The streptococcus pyogenes was recovered from the lungs and the vegetations and adherent clots in and about the aneurysm of the heart wall. The colon bacillus and two micrococci which could not be identified were also obtained from the lungs.

November 14, 1898.

DISCUSSION.

Dr. Hektoen—The subject of endocarditis has recently been thoroughly studied by Harbitz of Christiania. This author distinguishes between two groups of infectious endocarditis: 1, the endocarditis which is but a link in the pyemic process, the endocardial lesions being pronouncedly ulcerative, the embolic infarcts suppurating, and the clinical course rapid; the cases of this sort are commonly caused by staphyloccoci. 2, a more chronic endorcarditis, of insidious onset and slow progress, the endocardial changes being less destructive, the vegetations composed partly of thrombosis material and recent

connective tissue, and the resulting infarcts generally not the seat of suppuration; these cases are oftenest caused by the streptococcus and pneumococcus. It seems to me that the case described by Drs. Cotton and Le Count belongs to the second rather than to the first group. Harbitz found that, in the second group, the bacteria are generally found often in huge numbers, along the borders of the thrombotic masses.

ANEURYSM OF THE ABDOMINAL AORTA.

W. E. COATES.

The patient from whom the specimen was obtained was a man who had done heavy work most of his life. The family history furnishes nothing bearing upon the disease, and there is no evidence of alcoholism or syphilis. For two years before death, he had presented symptoms of a gastro-intestinal indigestion, with attacks of pain in different parts of the abdomen. Examination of the abdomen failed to reveal any tumor or swelling.

Death followed a few minutes after a very severe attack of pain in the abdomen. This final attack was preceded during 24 hours, by several paroxysms of less severe pain, accompanied by gastric disturbance.

The autopsy revealed nothing of interest outside of the aneurysm, and the results of its rupture. The peritoneal cavity was filled with blood. There was a large sacculated aneurysm of the aorta extending from the eleventh dorsal to the third lumbar vertebræ. The wall of the aneurysm was ruptured 2 cm. below the diaphragm. The sac measured 10 cm. in length and 5 to 8 cm. in diameter. Surrounding the sac in front and to the side was considerable laminated blood-clot, probably formed after a partial rupture several hours before the fatal termination. There was erosion of the bodies of the first and second lumbar vertebræ.

January 10, 1898.

SENILE ARTERIO-SCLEROSIS—"ATHEROMATOUS ABSCESSES" IN THE AORTA.

LUDVIG HEKTOEN.

The specimens consist of the heart, the aorta, and the large branches removed from a woman, 75 years of age, who died in the Cook County Hospital. The clinical diagnosis was bronchitis.

In the descending part of the aorta are many, variously sized subintimal cavities containing a greyish grumous material, some of these so-called abscesses have ruptured into the lumen presumably during the removal of the specimen. There were no symptoms of embolism observed during life. Many cavities are intact and the largest would contain at least a dessertspoonful of degenerate material. The internal covering is very thin and there is an entire absence of any thickening in the wall due to new fibrous tissue. There is no thrombosis in the aorta.

In the branches of the aorta are many areas of calcification. The heart is small and free from any fibrous changes.

Oct. 11, 1897.

D. N. EISENDRATH presented specimens: 1. Arteritis of common iliac with thrombosis and gangrene. 2. Congenital defect in heart of child. June 14, 1897.

C. W. F. READY presented hearts with tricuspid stenosis. June 14, 1897.

L. HEKTOEN presented specimens from an extreme case of senile atheroma. October 11, 1897.

J. A. CAPPS read a paper enittled "Aneurysms of the Coronary Artery." October 10, 1898.

THE DIGESTIVE SYSTEM.

PRIMARY CARCINOMA OF THE GALL-BLADDER ASSOCIATED WITH GALL-STONES; SECONDARY CARCINOMA OF THE LIVER.

JAMES B. HERRICK.

The walls of the gall-bladder were greatly thickened and made with the adjacent portion of the liver a mass the size of a large orange, shown by microscope to be carcinoma and believed to be the primary tumor. Numerous smaller, discrete nodules were scattered throughout the liver, this organ being greatly increased in size. Several facetted gall-stones were found in the gall-bladder suggesting the possible primary irritating cause for the development of the tumor at this point, though attention was drawn to the fact that according to some, the gall-stones in many such cases are to be looked upon as secondary and as due to the deposition of bile-salts from altered mural secretion owing to the involvement of the wall in the new growth.

The specimen was from a middle-aged woman who for several weeks had been losing in strength and weight, had suffered from severe epigastric pain and impaired appetite. The examination was negative, save for the emaciation, anemia and the enlarged hard liver, with irregular border and nodular surface. The ante-mortem diagnosis was carcinoma of the liver, presumably from the numerous nodules felt secondary. The possibility

of the trouble being primarily in the gall-bladder or ducts was considered. No history pointing to gall-stones could be elicited.

March 8, 1897.

HEMORRHAGE INTO AND ABOUT THE PANCREAS; ARTERIO-SCLEROSIS, PROBABLY SYPHILITIC; PECULIAR LOCATION AND RADIATION OF PAIN.

GEORGE H. WEAVER.

The case which is now reported occurred in the practice of Dr. E. I. Hook, and I am indebted to him for the opportunity of making the autopsy, and for the clinical notes.

C. H., aged 31; policeman; large and fleshy. Had never before had any sickness. Was a constant but not excessive user of alcoholics. There is a history of venereal disease, but none of syphilis. On the evening of May 10, 1897, he retired at 10 P.M., having eaten his usual supper and spent the evening about his home. He was apparently in perfect health, and slept well until 1 o'clock the following morning, when he was awakened by pain behind the middle of the sternum, which was very severe and radiated to the upper part of the chest, shoulders and arms. The pains continued in spite of local applications up to about 3 A.M., when Dr. Hook saw the case. At this time the patient complained only of pains as above described; temperature normal; no pain or tenderness in the abdomen. No tympany. Bowels had been regular. The condition was thought to be rheumatic. Under the use of hot applications and the administration of salicylate of sodium and small doses of deodorized tincture of opium, the pains continued. During the forenoon, up to 11 A.M., the patient, though very weak, sat up in a chair occasionally. He complained of his arms feeling as if they had been "chopped off." He swallowed some nourishment, but said it was hard to get it down. He only vomited when given medicine and brandy. He gradually became weaker, but his mind remained clear, and a few minutes before he died had talked with his wife. Death was sudden, occurring about twelve hours after the onset.

Autopsy, fourteen hours after death: Large, well developed man; much fat tissue; rigor mortis marked; much post mortem

lividity. Lungs negative. Heart muscle pale and flabby, cavity empty, valves and coronary vessels normal; aorta negative. Liver measured 12x8½x6 inches; it was dark from blood, otherwise negative. Spleen measured 16x10x7 centimeters, weighed 337 grammes, was soft and congested. The splenic artery seemed thickened, and the lining slightly irregular, with white spots; it was empty, as was also the vein. Kidneys were negative, except that cortex was rather wide, and they contained a large amount of blood. Adrenals, stomach, and intestines negative. On exposing the pancreas it was seen to be a dark purple color, and there was an accumulation of blood behind the peritoneum below the pancreas, extending to the upper end of the left kidney, and to the left a little beyond the end of the tail of the organ. The pancreas was soft and friable; its surface was of a dark mottled red and pink color, with small areas of a distinctly darker color.

On section, at both the head and tail the gland tissue was seen to be of a muddy grayish color. In the center of the body on section there was an infiltration of blood between the lobules, the pancreatic glandular tissue appearing yellowish in color, and more like normal tissue. This part was also firmer than the ends. No areas of fat necrosis were found anywhere. Cultures from the pancreas, liver, and spleen on agar and blood-serum were all negative. Microscopic examination of the tissues after hardening in alcohol and formalin, and staining in various ways, gave the following results: Kidneys showed distension of the smallest vessels with blood, and proliferation of the cells in capillary walls. Liver showed marked congestion of the capillaries of the lobule, with pigment deposit at the central part of the lobules especially. The central vessels were somewhat thickened and hyaline in appearance. The spleen showed marked congestion. Sections from the ends of the pancreas did not contain any normal gland structure. In places the gland tissue had almost entirely disappeared, and was replaced by more or less broken-down blood. In other parts the gland cells stained with eosin intensely, and lost their outlines. Scattered about in these latter areas were various sized fragments of nuclei, staining with nuclear stains. In these areas were seen homogeneous colloid-like bodies, staining faintly with nuclear stains, the exact nature of which was not determined. Sections from the central part of the organ showed the gland tissue to be more nearly normal, the infiltration with blood and the necrosis being confined to the periphery of the lobules. In all these sections of the pancreas the vessels, especially the larger ones, had very thick walls, some of them having no patent lumen. Transverse section of the splenic artery showed a thickening of intima in areas. No bacteria could be demonstrated in sections of the pancreas or spleen.

From the changes found in the vessels there was pres-

ent evidently an arterio-sclerosis, involving especially the smaller vessels in the liver and kidney, and also the larger vessels in the pancreas. The age of the patient, and the nodular character of the endarteritis in the splenic artery, would point to syphilis as a possible cause.

From the abundant and quite recent literature upon the subject it seems hardy necessary to discuss the question. It is, however, especially interesting to note the peculiar history as regards the location of the pains. No reference was made to the upper abdomen, but the pains were all referred to the upper part of the chest, shoulders and arms. This peculiar radiation of the pains I have not found noted in any of the numerous reports of cases.

The source of the hemorrhage would seem to be from rupture of some of the weakened vessels in or about the pancreas.

June 14, 1897.

CASE OF STRANGULATED INTERNAL HERNIA THROUGH AN OMENTAL SLIT.

W. I. BROWN.

The patient was admitted to Cook County Hospital Nov. 25, 1897. Six days before he was taken suddenly with a severe pain in the left thigh and abdomen, and at the same time began vomiting, which has continued more or less ever since, especially after drinking water; he had had no bowel movement since six days and has taken two cathartics. No history of similar attacks.

The general condition of the patient was bad. Pulse rapid, weak and compressible. The extremities were cold, cyanotic and covered with clammy sweat. The abdomen was distended, tympanitic, and slightly tender; no tumor mass or hernia could be felt. The patient's

condition grew rapidly worse and he died two hours after admission.

Upon opening the abdominal cavity which is distended by gas and fluid, the omentum is not seen, as it is displaced to the right and firmly adherent to the cæcum and the small intestine in that neighborhood. In the pelvis are numerous coils of small intestine which are completely collapsed and cyanotic. There is a point of obstruction in the median line, opposite the sacral promontory. On the under side of the omentum at this point is a slit which does not completely perforate the omentum, forming a band which is not larger than a sewing thread. Through this incomplete slit, coils of small intestine have passed until the true pelvis is full of collapsed cyanotic intestine. The distal end of the loop lies within 7 cm. of the ileo-cæcal valve and is freely movable, the proximal end being the one strangulated. The obstructing band has been carried down by the weight of intestine, which had passed through the slit, to a point opposite the attachment of the mesentery of small intestine to the spine. All of the intestine below the obstruction, both small and large, is collapsed except the cæcum. All the intestine above the obstruction is greatly distended by gas and dark brown fluid of fæcal odor, and the mucous membrane above the obstruction is apparently normal.

So far as the history and clinical manifestations of this case are concerned, there is therefore nothing unusual except the simplicity of giving him relief had the patient come to operation before he was moribund. The specimen is a classical, yet an unusual one. In examining the specimen, one is surprised at the strength of the small fibrous cord and one might well say that his life "hung on a thread."

Dec. 3, 1897.

A CASE OF NOMA IN AN ADULT, COMPLICATING AMEBIC DYSENTERY.

E. R. LE COUNT.

Although that form of gangrenous stomatitis to which the name noma refers is known to appear in connection with wasting and cachectic diseases, its combination with amebic dysentery, and in an adult, has not been previously noted, so far as I have been able to determine. The following is a brief report of such an occurrence[1]:

H. B., a barber, 35 years old, was taken ill in the early part of January, 1896. He was of somewhat dissolute habits, but had never been seriously ill. This illness began with a severe diarrhea, which persisted so that in the latter week of January he was having two, three, and four or more bowel-movements a day. The stools were made up of a thin, dark-greenish fluid, which was occasionally slimy or bloody. At this time the man was confined to bed, very weak, delirious at night, with a temperature of 101° or 102° F., and a pulse-rate that ranged between 120 and 140. He grew rapidly worse; delirium was replaced by periods of stupor; bowel-movements and urination became involuntary; and death took place February 2. Three days before death a discoloration of the lower lips was noticed, which gradually increased in size. It was of a dark-bluish color, sunk slightly below the surface and in marked contrast to the remainder of the face, which was pallid.

At the autopsy, the body was found to be that of a well-nourished, small man. Muscular development was poor, the surface of the body pale, the pupils equal, the hair and the beard black. There was marked rigor mortis. On the lip and chin were two gangrenous spots, which together equalled an area about 4 c.m. in diameter. On cutting through that on the lower lip, the dark necrotic appearance was seen to extend entirely through the lip—the mucous membrane being also black. The cheeks were swollen, and the upper part of the neck was edematous and of a cyanotic hue. The abdominal wall contained a layer of fat 3 or 4 c.m. thick near the navel. The diaphragm extended to the fourth rib on the right side, and to the fourth interspace on the left side. In the upper part of the abdominal cavity there were adhesions uniting the transverse colon to the abdominal wall, and the omentum to the anterior wall of the stomach; otherwise the peritoneum was smooth and its cavity empty. These adhesions were fibrinous and easily broken.

The pericardial cavity was full of a clear fluid, its surface smooth. The heart was of normal size, presented a rounded apex, a smooth endocardium, normal orifices, and it contained goose-fat clots. The anterior mitral leaflet was slightly thickened. The myocardium showed no changes. The beginning of the aorta was smooth. Adherent thrombi were found in both appendages. The pleural cavities were empty and the serous layers showed no adhesions, except at the right apex, and here the adhesions were firm, but few in number. Both lungs floated in water and crepitate; the posterior parts were edematous and congested.

The liver had a smooth external surface, and distinct lobular markings. It was of a light reddish-brown color and showed no abscesses or areas of necrosis, although many cuts were made in the organ. The gall-ladder and the biliary passages were normal. The kidneys showed some cloudy swellings.

The upper surface of the tongue was black, except around the edges. The lining of the soft walls of the entire buccal cavity was of a dirty black as far back as the rami of the jaw. The discoloration of the tongue stopped at the circumvallate papillæ. The tonsils showed no gross changes. The mucous lining of the larynx, esophagus and trachea were covered with a delicate, removable fibrinous exudate, but there was no erosion.

In the colon, beginning at the cecum with a few isolated ulcers, there was practically entire absence of the mucous lining. What remained showed as multiple polypoid tufts, a mass here, one there and between them smooth ulcers, with the muscular coats clearly exposed. In places where the ulcers were still discrete and separated by narrow bands of mucosa, they nevertheless communicated by submucous passages. The colon contained a considerable amount of bluish-black, semi-solid, putty-like, foul-smelling feces.

Examination of the brain was not allowed.

The anatomical diagnosis was: Ulcerative colitis; fibrinous peritonitis; gangrenous stomatitis; fibrinous laryngitis, tracheitis and esophagitis, cloudy swelling of the liver and kidneys; edema of the lungs (hypostasis).

Through an accident to the plates made from the heart's blood, liver and lower lip, complete bacteriologic examination was not possible.

On histologic examination heart, spleen, pancreas and lungs showed no important changes. In the liver a slight passive hyperemia of the lobules was present, with a considerable fatty deposit at the periphery. The liver-cells themselves seemed swollen, but the nuclear staining was uniform and good. The narrowed capillaries showed many polymorphonuclear leucocytes. In places marked round-cell infiltration had taken place

around the smaller bile-ducts, the accumulation of cells being most marked just external to the basement-membrane. There was no increase in the connective tissue, nor any large foci of round cells to mark minute areas of necrosis of liver-cells.

In the kidneys the glomeruli filled the capsule of Bowman with capillary loops engorged with blood. The convoluted tubes were lined with swollen epithelium; in many places the lumen appeared filled by the cells. There were also slight endarteritis and venous hyperemia, the veins of the cortex in particular appearing dilated.

In the colon the undermining ulcers were found to possess edges devoid of tubular glands, and made up of a mass of granulation-tissue that had in it numerous large thin-walled blood-channels. In these the blood was in places coagulated, distinct masses of fibrin marking the clotting. The ulcers extended in many places down to the circular muscular coat, which also contained dilated vessels and numerous areas of round cells. Amebæ were easily demonstrated by thionin and methylene-blue staining, both in the granulation-tissue of the edges and in the blood-channels.

The trachea and esophagus showed loss of the epithelium, slight superficial necrosis in places, and hyperemia of the vessels of the submucous coats. The tongue, which was black, exhibited no change other than a desquamation of the superficial epithelium and a thick deposit on its surface of a brownish débris made up doubtless of necrotic material.

A section of the lower lip through the gangrenous area was found to consist of tissue that was entirely necrotic, all the structures being uniformly affected. The structural outlines of muscle, glands, and other elements were preserved, but all alike were wanting in nuclei that stained. In this necrotic tissue were swarms of short, slender bacilli, two and three times as long as thick, and very numerous at the edges of the necrotic tissue. Here there was slight reaction, the line between necrotic tissue and healthy tissue being quite sharp. The bacilli stained by Gram's method.

There can be no doubt, from the anatomic appearance of the necrosis of the lip and chin, that the lesions in this case belong to those described as gangrenous stomatitis; further, Babes and Zambilovici[2], Grawitz[3], Foote[4], and Bishop and Ryan[5], as well as others have called attention to the peculiarity that in noma the necrotic tissue literally *swarms* with bacilli.

The rarity of noma in an adult is apparent from the statistics of Kruss[3]. Collectively considered, among

165 cases, 68 per cent. occurred before the fifth year of age, and 30 per cent. between the ages of 5 and 15.

Great confusion has prevailed concerning the specific bacteriologic agent in noma. Bearing upon this feature the researches of Babes and Zambilovici are most important. Noma is not an infrequent disease in Bucharest, as these observers report seeing 6 cases in five months. In the two cases that they were permitted to investigate, they found a slender bacillus that caused gangrene in the cheeks of rabbits. In other animals, septicemia or abscesses were produced. The bacillus grows well on most media, liquefies gelatin, and decolorizes by Gram's method. In most cases there was marked anemia, and both cases were preceded by measles. Histologically, the observers named found that the bacilli at the edges of the necrotic tissue stain better than those in the central portions; also, that there occurs a dense accumulation of leucocytes in advance of the necrosis, and they are inclined to believe that the crowding of the vessels by these favors necrosis. Guzzetti[7] studied 4 cases of noma, and in 3 of them found a bacillus that he considered as identical with that described by Babes and Zambilovici. It is of exceeding interest to note in this connection that Freymuth and Petruschky[8] have recorded a case of noma genitalium, in which the diphtheria-bacillus was found, and recovery followed the use of antitoxin. The same observers[9] report a case of noma of the face in a child, 8 years old, following typhoid fever. In this case the diphtheria-bacillus was present and the junction with the pseudodiphtheria-bacillus and the staphylococcus aureus. These observations seem to indicate that although noma may, in the majority of cases (at least that form occurring on the face), be due to a specific bacteriologic agent, some cases of gangrene or necrosis occur that, for the present, at least, must be included under the term noma and that are due to

other bacteria. From the domain of comparative pathology[10] we have a confirmation of this possibility in the work that has been done with the necrosis-bacillus (Bacillus necrosis, Salomonsen; Streptothrix cuniculi, Schmorl; Bacillus necrophorus, Flügge), which has been found in various forms of gangrene and necrosis in cattle, horses, swine, deer, the kangaroo, antelope, the house-mouse, and rabbits. The study of the microscopic changes produced in the tissues shows that this organism also is found in profusion in the zone between dead and living tissue; that it evidently produces a strong and virulent poison, and that it does not thrive in the tissue that becomes necrotic. Further, in the necrotic tissue, great numbers of various bacteria are present, but few necrosis-bacilli. The necrosis-bacillus, however, is an anaerobe.

January 10, 1898.

BIBLIOGRAPHY.

1. For the opportunity to make the autopsy in this case and for the abstract of the clinical history, I am indebted to Dr. Boucsein of Chicago.

2. v. Babes and A. Zambilovici: Recherches sur le noma. Annales de l'Institut de Pathologie et de Bacteriologie de Bucharest, vol. v, 1892-93, p. 227.

3. Grawitz: Demonstration eines Falles von Noma. Deutsche med. Wochenschrift, xvi, 318.

4. Foote: Report of a Case of Gangrenous Stomatitis, with a Bacteriological Examination. Am. Jour. of Med. Sci., n. s. cvi, pp. 198–207, 1893.

5. Bishop and Ryan: Noma and Allied Diseases of the Mouth, Report of Three Cases with Pathologic Examination. Transactions of the Chicago Pathological Society, vol. i, p. 252.

6. Krauss: Specielle Pathologie und Therapie, Nothnagel, Bd. xvi, Th. 1, Abth. 1, p. 202.

7. Guzzetti, P.: Richerche bacteriologiche e istologiche sul Noma. Policlinico, vol. iii, No. 18.

8. Freymuth and Petruschky: Ein Fall von Vulvitis gangrænosa (Noma genitalium) mit Diphtheriebacillenbefund. Behandlung mit Heilserum; Heilung. Deutsche med. Wochenschrift, 1898, No. 15.

9. Idem: Zweiter Fall von Diphtherie-Noma (Noma faciei). Behandlung mit Heilserum; Herstellung. Deutsche med. Wochenschrift, 1898, No. 38, p. 600.

10. O. Lubarsch und R. Ostertag: Ergebnisse der allegemeinen Pathologie und pathologischen Anatomie des Menschen und der Thiere, ii, 1895, p. 122.

CONGENITAL OCCLUSION.

A CASE IN THE DUODENUM WITH AXIAL TWISTING AND FIBROUS PERITONITIS, ASSOCIATED WITH CALCAREOUS MASSES AND PECULIAR GIANT-CELL-LIKE BODIES.

J. L. STEWART.

Although congenital occlusion of the small intestine is not of frequent occurrence, the subject has, of course, been thoroughly studied, and in reporting an additional case of this kind one can therefore scarcely expect to advance anything new. The subject is, however, of greater interest now than formerly, on account of the recent rapid advance in intestinal surgery, which offers the only chance of saving the life of these otherwise usually well developed infants.

Congenital occlusion of the intestinal canal may occur anywhere throughout its extent. The most frequent site of occlusion is, according to Rokitansky[1], in the rectum; the present case, however, concerns the small intestine, to which attention is therefore limited. According to Theremin[2] the most frequent site of occlusion in the small intestine is in the duodeum, the next most frequent is near the ileocæcal region. Three cases have been reported by Hudson[3] in which the stenosis occurred exactly thirty-six inches from the ileocæcal valve. A number of cases have been reported in which the stenosis occurred near the ileocæcal valve, usually within twelve inches. One case is reported by Wilks[4] in which the stenosis occurred directly opposite the ductus communis choledochus.

In connection with the site of occlusion the observation of Corini[5], that the intestinal canal is developed in sections, is important. The first section extends from the mouth to the duodenum, the second from the duodenum to the cæcum, and the third from the cæcum to the rec-

tum. This might in a measure explain the frequent occurrence of occlusions in the duodenum and ileocæcal region; however, it would not explain the occurrence of occlusions in other locations, so that in a great many cases other causes must be sought.

Amniotic bands are said by some, the most notable being Schmidt[6], to be a possible cause; there is nothing in common, however, between the amniotic and pleuroperitoneal cavities (Küttner[7]).

Ulcer has been advanced by Wilks[4] as a possible cause of congenital stenosis. It is not difficult to understand how an ulcer could produce a stenosis, yet the occurrence and causes of intestinal ulcers in the fetus are subjects of which extremely little is known. Küttner[7] says circular ulcers may be explained as due to strangulation by the mesentery.

Diverticula may be the cause in one of two ways: first, as described by Mr. Bland Sutton, by excessive closure, as in the three cases reported by Hudson[3]; secondly, by the diverticula becoming attached in such a way as to cause constriction, as in the case of fibrous bands leading from the umbilicus, which sometimes become detached and later adhere to other parts of the abdominal cavity, causing constriction and occlusion. One such case is recorded in Ziemssen's Cyclop., vol. vii, p. 537.

Embolism of the mesenteric artery might cause stenosis, because of anemic necrosis and subsequent chronic fibrous replacement, and it would seem fairly rational to put that as a cause in certain rare cases where there are endocardial lesions or other conditions that could lead to embolism. Durante[8] reports a case in which he thinks it possible that an endarteritis of the mesenteric artery lay at the bottom of the condition. Brindeau[9] assigns a separation and total occlusion of the duodenum as incident to the peculiar manner of development of the mesenteric artery, which cuts the intestine into two parts. In cases, like the one reported by Thomas,[10] where

there is an absence of a large part of the intestine (jejunum, ileum, and part of the large intestine), it would seem that the occlusion of the mesenteric artery might play an important part.

Intra-uterine peritonitis is regarded as a quite common cause of congenital stenosis of the intestinal canal. Fliesberg,[11] Craig[12] and Thomson[13] have reported cases in which there was fetal peritonitis. In the case reported by Craig there was a fibrous band arising from the intestine opposite the mesenteric attachment; the other end of the band was free. It is suggested that this was a piece of omentum which became attached by the inflammatory process. Thomson[13] and Hudson[2] report cases in which they say there was probably a patch of peritonitis which caused adhesions to the neighboring mesentery. W. M. Thomas[14] describes a case in which there were firm bands present. Hobson[15] describes another case in which he says there were no signs of peritonitis present, but the coils were everywhere adherent by fibrous bands. Fliesberg[11] also describes a total occlusion of the cæcum in which there was undoubted fetal peritonitis.

Küttner[7] and Gaertner[16] dwell much upon the importance of axial twist as an etiological factor in congenital occlusion of the intestinal canal. Gaertner[16] reports thirteen cases which are used to illustrate this mode of causation. The condition most favoring axial twist is a broad, high mesentery with a narrow shaft. Abnormally long peritoneal ligaments with excessive accumulation of meconium, causing violent peristalsis, naturally tend to produce twists. Aside from the axial twists in Gaertner's[16] cases, there was in Cases 2 and 13 of his series a fetal peritonitis, scaid to be secondary to the twisting. In Case 12 there was an alveolar carcinoma of the left lobe of the liver which overgrew a portion of the intestine, which was adherent to the liver and occluded. Küttner[7] reports a case in which he favors

axial twist as a cause. In this opinion Rokitansky[8] agrees.

Other causes of occlusion are mentioned by various writers. F. C. Turner[17] describes a membranous diaphragm in the middle of the jejunum. Twenty-one cases are reported by Gaertner[16] in which inguinal hernia was the apparent cause.

The clinical histories of most of the cases are almost uniform. The infants lived from one to six days. In two of Gaertner's[16] cases the patient lived ten days. The symptoms were those of intestinal obstruction, no fecal passages, persistent vomiting, and in some cases icterus from retained bile. Such symptoms in an otherwise apparently well-formed child would seem to justify the diagnosis of intestinal occlusion, and, as in the case to be recorded, surgical intervention should be resorted to early in the hope that the conditions may be so simple that the lumen may be restored.

The specimen to be described was sent to the Pathological Laboratory of Rush Medical College by Dr. J. R. Eastman, of Pleasant Prairie, Wis., to whom we are indebted for the clinical facts. The child, a male, was born of healthy parents, so far as known. The labor was normal. Soon after birth the apparently healthy child began to vomit. The vomitus was at first a dark-colored fluid, but as it continued this became thicker and of a dark green color. The vomiting kept on four days, during which time there were no bowel movements. On the fourth day a laparotomy was performed, a dilated portion of the gut opened, the contents evacuated, and the gut stitched to the margins of the opening in the abdominal wall. The child rallied from the operation and lived about twelve hours, during which time the vomiting ceased. The advantage of a complete post-mortem examination is lacking. The specimen at hand consists only of the stomach, large and small intestines, torn adhesions, and a part of the mesentery, in weak alcohol.

The examination of the specimen shows the stomach to be of normal shape, about six centimeters in length and about two centimeters in breadth. The pylorus is firm and about five millimeters thick. At a distance of about six centimeters from the pylorus the duodenum becomes dilated to a diameter of about three centimeters. The dilatation continues for about thirty centimeters and ends abruptly in a blind extremity one-half inch from which is seen the artificial opening in the intestine made at the operation. Near this blind extremity, and separated from it by a free edge of mesentery, about one inch in length, is seen the beginning blind end of the lower segment of small intestine, which seems to correspond to the beginning of the jejunum. The jejunum and ileum are one hundred and ten centimeters in length and one centimeter in diameter, varying only slightly throughout their extent. The vermiform appendix is two millimeters in diameter and five centimeters long. The cecum is only slightly larger than the appendix, and the large intestine only four millimeters in diameter, the length being about forty-five centimeters. The walls of the large and the small intestines below the occlusion are comparatively thin. The lumen contains a yellowish-gray, mucoid-like material. The wall of the upper dilated portion is somewhat thickened. In the lumen is seen some dark-greenish, grumous material. The occluded ends of the two segments, formed by the separation, seem to have twisted around each other in a spiral manner, as if the upper blind end of the jejunum had projected upward and to the left in the abdominal cavity, and the descending blind end of the duodenum had wound itself about the first ten centimeters of the jejunum, from below upward (see illustration). In connection with this spiral twisting of the intestinal tube there is also a twisting of the mesentery. The mesentery is not divided, but there is a shallow cleft, the edges of which are about one inch

in length, between the blind ends of the two segments. The lymphatic glands are everywhere enlarged, some the size of a large bean. The intestines are universally bound together by abundant firm fibrous adhesions.

Microscopic specimens were taken from the mesentery, lymphatic glands, adhesions, and large and small intestines. The secretions were stained with hematoxylin and eosin. Sections of the large and small intestines show a well preserved serous coat, on the outside of which is quite an abundant deposit of ragged fibrous tissue. The mucous membrane can not be demonstrated, and in its place is seen a mass of peculiar mucoid material, in the form of a quite regular network; it takes the hematoxylin quite well. The mesentery is seen to be covered with a ragged fibrous material. Between the layers are seen irregular masses of deeply-stained material, which, when they were cut with the microtome, were distinctly gritty, calcareous material. Among these masses a number of small brownish-green granules are seen—probably hematogenous or bile pigment. The walls of the blood-vessels are thicker than usual and the vessels are surrounded by much fibrous tissue. Between the layers of mesentery and among the calcareous bodies above described are seen a number of rather peculiar, irregular, circular bodies, which contain in their interior a number of smaller dark bodies that resemble nuclei. These bodies may be old and degenerated giant-cells, but positive statements can not be made, owing to the poor preservation of the specimen and consequent poor staining properties. The examination of the mesenteric glands shows no changes except the poor affinity for nuclear stains. The adhesions under the microscope are seen to be made up of irregularly arranged connective tissue fibers. Sections of the mesentery were stained by the Ziehl-Nielson method for the tubercle bacillus, and a diligent search made for this organism, but none were found.

Accompanying the occlusion are two conditions, each of which would seem to have some bearing on its ultimate cause, namely, the results of the fetal peritonitis present and the twisting of the intestinal ends as described above. In the mesentery are seen deposits of calcareous material and either hematogenous or bile pigment, and finally the peculiar bodies described in the mesentery that somewhat resemble giant cells, and the suspicion of a healed fetal tuberculous peritonitis is aroused. In the absence of positive proof, viz., demonstration of the tubercle bacillus, this question can not be decided. The peritonitis, of whatever nature it may be, may have been primary or secondary to the cause of the occlusion. It may be assumed with Valenta[18] and others that axial twisting occurred, followed by occlusion and peritonitis. Perhaps mechanical or other stenosis of a branch of the mesenteric artery ended in necrosis and perforation of the intestine at the seat of the present gap in its continuity, the fibrous peritonitis and calcareous and other bodies being the result of the extravasation of intestinal contents into the peritoneal cavity. The early period of development at which the defect in this case must have occurred renders the latter view rather improbable.

BIBLIOGRAPHY.

1. Rokitansky: "Abnormities of Intestinal Canal," Path. Anat.
2. Theremin: Deutsche Zeitschrift fur Chirurgie. 1877.
3. Hudson: Tr. Path. Soc., London, 1889, xl, 98-105, 1 pl.
4. Wilks: Tr. Path. Soc., Lond., 1861, xii, 102.
5. Corini: Internat. Klinische Rundschau, Wein., 1890, iv, 195.
6. Schmidt: St. Petersburg Med. Zeitschr., 1870, N. F. i, 565; 1871 N. F. ii, 102-4.
7. Küttner: Virchow's Archiv., liv, 34.
8. Durante: Bull. et Mem. Soc. Obst. et Gyn. de Par., 1897, 51.
9 Brindeau: Bull. et Mem. Soc. Obst. de Gyn. de Par., 1895, 73.
10. Thomas: Lancet, Lond., 1884, i, 63.
11. Fliesberg: Northwest Lancet-Clinic, St. Paul, 1891, xi, 333.
12 Craig: Tr. Edinb. Obst. Soc., 1881, vi, 146-150.
13. Thomson: Edinb. Med. J., 1891-2, xxxvii, 840-5, 1 pl.
14. W. M. Thomas; British Medical Journal, Oct. 20, 1886.
15. Hobson: British Medical Journal, Lond., 1893, i, 637.
16. Gaertner: Jahrb. f. Kinderh., Leipzig, 1883, N. F. xx, 403.
17. Turner: Tr. Path. Soc., Lond., 1887, xxxviii, 145.
18. Valenta: Jahrbuch fur Kinderheilkunde, viii, 1864.

A CASE OF SIMPLE HEMANGIOMA OF THE UPPER PART OF THE SMALL INTESTINE.

LUDVIG HEKTOEN.

The specimen which consists of the upper third of the small intestine, was removed from the body of a forty-eight-year-old man, who died in consequence of chronic aortic and mitral endocarditis with an acute exacerbation. As can be seen, there are many large vessels running underneath the mucous coat, and as a general rule transversely to the long axis of the intestine and parallel to each other, giving the mucous membrane an appearance as though it were the seat of varicose veins.

Between a few contiguous vessels are occasional small anastomoses, but by far the greater number of the vessels seem independent of each other. In some parts, especially where the vessels are the largest, there is considerable actual overlapping, but elsewhere they are separated from each other by distances varying from one to two cm.

The smaller vessels especially present numerous nodular enlargements, all of which are filled with blood and project beneath the mucosa.

The mucous membrane is normal, and there are no changes in the veins of the mesentery or other part of the abdominal viscera. Microscopic examination of the structure of the vascular growth shows it to consist of abnormally numerous and abnormally enlarged veins, with saccular and globular dilatations.

January 10, 1898.

STRANGULATED INTERNAL HERNIA THROUGH A MESENTERIC HOLE.

LOUIS J. MITCHELL.

J. F., a boy eight years old, was sent on an errand on January 17th. He ran down the outside stairs, and when near the bottom the guard rail gave way and he fell into the yard, striking on his abdomen on the frozen ground. The boy picked himself up and went back to his mother, told her of the accident, and then completed the errand. Nothing further developed until the morning of the 19th of January, when he complained of severe pain in the abdomen; a physician was called in, who diagnosed peritonitis, but unfortunately instituted no operative measures. Death ensued on January 21st.

The necropsy showed an opening in the mesentery near the ileo-cecal junction which presented smooth margins. Several loops of bowel had passed through this and had become strangulated, being dark cherry red in color. The parietal peritoneum in the vicinity was red also and had some flakes of lymph on its surface. The examination revealed no further facts bearing on the case.

Mr. Treves, in the Hunterian Lectures for 1885,[1] explains the formation of these holes.

"In the fœtus," he says, "it will often be observed that the ileo-colic branch of the superior mesenteric artery circumscribes by its anastomosis with the last of the intestinal arteries an area on the mesentery of a well rounded or oval shape. This area is remarkable in so far that it presents no fat, no visible blood vessels of any kind, even in well injected specimens, and is never occupied by any mesenteric glands." A little further on he adds: "It will be seen that this area has the precise situation, the outline and the dimensions of the mysterious mesenteric hole, and by the atrophy of the peritoneum

[1] The Anatomy of the Intestinal Canal and Peritoneum in Man.

occupying the district such a hole would be formed." The author then describes a case where this areas was entirely devoid of fat, while the surrounding mesentery was quite opaque from the depositing of fat, and the writer has also noted a similar case.

During the writer's service as coroner's physician, in considerably over one thousand necropsies, genuine holes were met with only three times, or one in over five hundred cases. The first was a male child at term, in whom the opening was circular and one-half inch in diameter. The second was in a man of 24; here the aperture was located in the same region, the ileo-cecal junction, but was elliptical, measuring one by three-quarters inches. In the third case, a woman of 45, had an elliptical hole in the mesentery of large size, 1 by 1⅞ inches. Like the others, it was situated near the union of the small and large intestines, and the upper end was partly occluded by a thin membrane, ⅜ by ⅞ inches. In none of these three cases was the cause of death connected with the presence of the holes.

In the case of the little boy, first described, of course it is impossible to determine whether the hole was entirely open, or whether it was closed in by a cribriform membrane, such as Mr. Treves alludes to, and the traumatism forced the bowels through the perforated layer.

This variety of internal strangulation, while not exactly rare, is somewhat uncommon, and it would seem that the explanation is furnished by the comparative infrequency of the mesenteric holes.

January 10, 1898.

CARCINOMA OF THE PHARYNX, WITH EXTENSIVE AND ERRATIC CORNIFICATION.

LUDVIG HEKTOEN.

Under the microscopes are placed a number of sections of carcinoma characterized by an unusually extensive and erratic cornification. The tumor in question was removed after death from a man of about 45, who died in the Cook County Hospital. The revised anatomical diagnosis is as follows:

Carcinomatous ulcer in the left sinus pyriformis; metastatic growth in the right side of the neck and in the liver; lipoma of the stomach; diffuse bronchitis and bronchopneumonia, purulent pleuritus, arterial sclerosis, and chronic nephritis.

The right half of the epiglottis and the adjacent pharyngeal mucous membrane were the seat of an irregular ulceration whose margins were raised and notched, the floor containing larger and smaller yellowish points; the anterior margin extending down into the beginning of the esophagus. The ulcer measured about 6 cm. vertically and 3 cm. transversely, being of an oval outline. On the right side of the neck, one inch above the middle of the clavicle, was a firm, oval growth, about as large as a walnut, firmly connected with the deeper parts, the skin, however, being freely movable. Dissection showed that the growth was not connected with any of the adjacent muscles, that it was irregularly oval and nodular, of grayish color, but containing small masses of yellowish, caseous-like material. In the right margin of the right lobe of the liver was a small, subcapsular district, composed principally of cicatricial tissue enclosing whitish or yellowish masses, the whole being about as large as a hazel-nut. Just below the gastro-esophageal junction was a small, oval mass in the submucous tissue of the stomach, which on microscopic examination proved to be a lipoma. The other organs did

not present any changes of interest in this connection.

It is only proper to say that, on account of the similarity of some of these lesions to syphilitic changes, they were at first, before microscopic examination had been made, regarded as of syphilitic nature, and this was so stated in the original anatomical diagnosis. Perhaps the subcapsular area in the liver and the submucous mass in the stomach had the most to do with the formation of this diagnosis. Microscopic examination, however, showed the nodule in the stomach to be a lipoma,, and the ulcer in the sinus pyriformis, the mass in the of an unusual structure because of the excessive cornification.

While the ordinary stains gave quite satisfactory results, it was, nevertheless, very fortunate to have at hand a reasonably reliable method for staining the horny material, namely, Gram's method. This useful method, first suggested for this purpose by Babes[1] is, as recently shown by Paul Ernst, an almost specific stain for horny material. Ernst was first led to its use for this purpose in an effort to demonstrate horn in a flat-celled carcinoma of a bronchus.[2] Subsequently he described his studies of hornification with Gram's method under normal and abnormal conditions in two articles[3] in which special details may be sought.

It has been found that, generally speaking, the violet color given horn by Gram's method materially aids in recognizing beginning and limited hornification, and also in studying the relation of kerato-hyaline granules to the cell and to the fully-formed, more or less lamellar horny substance. In the present case the method brings out most clearly the unusual extent and lawlessness of the hornification in the tumors, whose nature, on this account, at first seemed rather obscure.

As may be seen in the specimens, the growths consist of a connective-tissue stroma, with many small-celled masses of rather small, compressed, flat epithelial cells,

irregularly mixed with horny material, and also large and variously shaped districts, composed wholly of horn, of a wavy fibrillar, lamellar or scaly structure, and often surrounded by a zone of small round cells. Often very small groups of epithelial cells have been partly or wholly changed into horn and a few quite characteristic pearls are to be seen in the midst of connective tissue, showing that hornification has occurred in all the cells of the nest. Sometimes masses of epithelial cells are seen with cornification taking place at the periphery instead of the center.

In the growth in the neck (which occupies a group of lymphatic glands, and must, therefore, be regarded as a secondary, and not as a possible branchiogenous carcinoma), the erratic and widespread cornification is most well-marked. There are areas, corresponding apparently to a whole lymph-node, and occupying the major part of the sections, composed of irregular, scaly masses, which, in part, stain a diffuse deep-violet with Gram's method, in part remain unstained, or stain with the carmine or with hematoxylin. At other places the lymph-follicles contain, instead of small groups of carcinoma-cells, minute accumulations of horny material. In the mass in the liver the hornification has not been so extensive, but here also it has occurred in an anomalous manner. In the pharyngeal ulcer the hornification is also very extensive, and the resulting material has a much more concentric, parallel and wavy, fibrillar appearance than elsewhere. The surface of the ulcer is the seat of necrosis, and below there is marked leucocytic accumulation.

The study in the early stages of hornification in these specimens is not satisfactory. The unusual rapidity and extent of the process may account for the absence of, or failure to find, good intermediate stages. As Ernst has pointed out, Gram's method does not always stain everything that looks like horn and in these sections are also

many places in which the horn-like material remains unstained.

The general lawlessness of carcinoma is, it seems to me, exceedingly well illustrated in the erratic and uncontrolled hornification in the primary and secondary foci of this tumor.

January 10, 1898.

BIBLIOGRAPHY.

1. Ueber einige pathologisch-histologische Methoden, Virchow's Archiv., 105, 1886.

2. Ein verhornirender Plattenepithelkrebs des Bronchus: Metaplasie oder Aberration? Ziegler's Beiträge, xx, 1896.

3. Archiv. für Mikroskopische Anatomie. Band xlvii.

Studien über pathologische Verhornung mit Hülfe der Gram'schen Methode, Ziegler's Beiträge, xxi, 1897.

CARCINOMA OF THE STOMACH, RETROGRESSIVE LYMPHATIC TRANSPORT, MULTIPLE CARCINOMATOUS CONSTRICTIONS OF THE ILEUM AND TRIPLE SIMULTANEOUS PERFORATIONS.

W. C. F. WITTE.

Mr. H. was admitted to the Presbyterian Hospital of Chicago on Nov. 19, 1896, under the care of Dr. N. Bridge, and later of Dr. John A. Robinson. His family history was good. The father was drowned, and his mother is still living in Finland, where she is enjoying good health. His brothers and sisters are all living and well. There was no history of syphilis, tuberculosis, or malignant tumor. The patient was 43 years old, married, and a miner by occupation. During childhood he had the diseases usually occurring at that time. From that period until this illness she had no serious disease. His habits were good, and he used alcoholics but moderately. His present trouble was first noticed during October, 1895, at which time he experienced a sharp pain, located at the pyloric end of the stomach, and radiating laterally. This pain was more or less continuous during the entire illness. Vomiting did not occur until some time during October, 1896, after which it was continuous. The vomitus consisted of food taken, and mucus which was sometimes stained with blood; the vomiting usually occurred many hours after eating. From the beginning of his illness, in 1895, up to the time he entered the hospital, he had lost 30 pounds in weight. His appetite was very poor,

and he had taken mostly liquid food. The bowels were constipated. When he entered the Hospital on Nov. 19, 1896, he was conscious and confined to bed. Movements of the extremities were carried out with great difficulty; his body was emaciated, and the skin dry and flabby, having a peculiar lemon-color. The respirations were normal; his tongue was thickly coated and furred. The pupils were equal, the sclerotics slightly jaundiced. The abdomen was not distended, and there was no ankle-edema. The physical examination of the thorax was negative. On palpating the abdomen it was found to be tender on deep pressure, especially near the pyloric end of the stomach, but no distinct mass could be outlined. There was no enlargement of the liver or spleen; a little tympanites was found on percussion. The outlines of the stomach did not extend below the umbilicus. A test-breakfast was given, consisting of a cup of tea and a biscuit. One hour later the contents of the stomach were removed and analyzed. Four ounces of fluid were obtained. Uffelmann's test showed the presence of lactic acid. Günzburg's test showed deficient digestive power. Absorption-test required 12 minutes; the reaction of the material was acid. Urine examination negative.

The patient was shown in the Medical Clinic of Rush Medical College by Dr. N. Bridge, and a diagnosis of carcinoma of the pylorus was made.

The treatment consisted of daily lavage, liquid food, and stimulation by means of drugs.

On November 26, a week after his admission to the hospital, the patient had a sudden sharp pain in his abdomen,, continuing for several hours. His pulse became irregular, rapid and feeble. The abdomen became distended, constipation was complete, and tympanites developed. A diagnosis of peritonitis from perforation was made. Six days after the attack the patient died, and three hours later a post-mortem was made by Dr. Hektoen.

Post-Mortem Report.—The body was still warm, of medium size, and somewhat emaciated. The hair was yellowish, the neck long and thin, the chest broad; the abdomen was distended and hard to the touch. The abdominal cavity contained a large amount of turbid, yellowish fluid. The peritoneal surface of the intestines was covered with fibrinous masses, and the coils were closely matted together. The left pleural cavity was obliterated by firm adhesions. The pericardium was smooth and empty. The heart was of normal size, and the endocardium smooth. On section the myocardium was firm and uniformly grayish-red in color. The left lung showed marked white thickening of the pleura, especially over the lower lobe. The right lung was firmly adherent, especially to the diaphragm. Both lungs contained much blood, and there was crepitation. The esophagus was smooth.

In the center of the lesser curvature of the stomach was a large nodular mass, the posterior surface of which was adherent to the liver. Owing to the constriction of the central part of the stomach by this mass, the stomach was drawn up into an hour-glass shape. On the mucous surface of this mass was an irregular ulcer, with rough, hard borders, and a smooth, hard floor. This ulcer extended half way through the stomach wall. The remainder of the gastric mucous membrane was normal.

The lymphatic glands behind the stomach were firm and nodular.

At 2, 5, and 7 feet above the ileocecal valve were constrictions of the lumen of the ileum, with corresponding perforations of the wall. The constriction nearest the ileocecal valve was the most marked externally, having the appearance of a healed intussusception. Just above the upper rounded end of this constriction, at the bottom of the sulcus forming it, and opposite the mesenteric attachment of the intestine, was a perforation about the size of the end of a small lead-pencil.

The mesenteric glands were distinctly enlarged, and on the peritoneal surface of the bowel were several grayish-white nodules about the size of a split pea.

On exposing the mucous membrane of the intestine, a narrow circular ulcer, 2 cm. in width, was seen, causing almost complete interruption of the continuity of the intestine, the continuity being maintained by a small band of tissue near the mesenteric attachment. In the center of this ulcer was the perforation mentioned. The margins of the ulcer were raised and thickened, of a darker color than the tissue adjacent to it. The floor and margins of the ulcer were nodular, most so at the margins and becoming less so toward the center, where the ulceration had extended through the different layers of the intestine. For quite a distance above the constriction the walls of the ileum were greatly thickened, apparently from an increase in the internal muscular coat and muscularis mucosæ.

The second ulcer corresponded in general to the one just described.

The third ulcer was less marked than the other two and apparently of more recent origin.

Higher up in the intestine was a fourth ulcer about the size of a silver 3-cent piece. It involved only the mucous membrane of the intestine, and externally no evidence of the ulcer was to be seen.

At various points in the small intestine were small irregular areas of infiltration, located principally in the submucous and subperitoneal tissue. The largest of these areas measured 1 cm. in diameter, and the smallest areas could barely be seen or felt.

The vermiform appendix was intact. The colon contained

hard fecal matter; its mucous membrane was smooth and normal. The retroperitoneal glands were enlarged. The capsules of the kidney were free, the substance firm in consistence, and the cortical markings very broad and distinct. They were of normal size and contained much blood. The adrenals, the liver, spleen, and pancreas presented no macroscopical changes, but there were adhesions between the liver and diaphragm and around the gall-bladder, binding the latter to the stomach and omentum. The aorta was smooth throughout its entire course. The brain and spinal cord were not examined.

The anatomical diagnosis reads carcinoma of the stomach; carcinoma of the regional lymph-nodes; multiple carcinomatous nodules and ulcers in the ileum, with triple simultaneous perforation; general sero-fibrino purulent peritonitis; chronic nephritis; right adhesive pleurisy; adhesive perihepatitis.

The feature of most interest in this case is the method in which metastasis occurred. There are at least four ways in which these secondary foci might have developed:

1. They might have occurred by way of the blood-current, but the absence of tumors in the liver, the lungs, and elsewhere, points strongly against this being the case.

2. The growths in the intestine might have been the result of a contact-infection, tumor-cells being carried with the gastro-intestinal contents from the stomach to the point of the ileum involved.

3. The secondary growths might have been the result of direct and continuous infiltration in the intestinal wall from the primary focus.

4. A retrograde lymphatic current might have carried the carcinoma-cells to the different points of localization.

That retrograde currents do occur in the lymphatics and blood-vessels has been shown by von Recklinghausen[1] and corroborated by many other pathologists, among them Karl Virth.[2] As long ago as 1867 Waldeyer[3] described the following instructive examples of this mode of metastasis:

1. A retrograde carcinomatous injection of the chylous vessels of the duodenum.

In a case of carcinoma of the pylorus it was found that in

the adjacent parts of the duodenal mucous membrane nearly all the chylous vessels of the villi were crowded full of epithelial cells. Many of the villi had retained their natural size, others, owing to the mass of the cells in their interior, were thinned and sacculated. Leading from the base of the villi out through the mucosa and submucosa and muscularis of the duodenum were streaks of epithelial cells which seemed to occupy the paths of the lymphatic vessels of the intestinal wall.

2. Retrograde metastasis of the peritoneum and mesentery in a case of carcinoma of the stomach.

Located on the small curvature of the stomach was a thick induration about the size of a dollar, over which the mucous membrane was intact and freely movable. From this there arose several secondary nodules, which, owing to their softness, were recognized as being of more recent origin. Microscopically the lymph-vessels throughout the muscularis of the stomach were filled with carcinoma-cells. The peritoneum, both visceral and parietal, was much thickened, as was also the suspensory ligament of the liver. Many small, flattened, non-transparent nodules, firm to the touch, were found. They were very abundant on the serous coat of the small intestine, and on the diaphragm were recognized many similar masses in the course of the lymph-vessels, which in some places led from one mass to another. On the pleural surface of the diaphragm were recognized many similar neoplastically injected lymph-vessels. It was impossible to follow them into the thoracic duct.

Another case of great interest in this connection is reported by Anton Brosch:[4]

There was found a primary carcinoma of the stomach, with two metastatic foci 5 cm. and ½ meter above the ileocecal valve, and one constriction in the vermiform appendix. In this case there was a single perforation in the primary tumor, which was attributed to a gastric ulcer coexisting with the carcinoma. The constriction nearest the ileocecal valve was so marked that the lumen of the bowel was not larger than a small lead-pencil. The mucous membrane was intact, and there was much hypertrophy of the bowel, due almost entirely to thickening in the muscular coat. The remaining constrictions in the bowel and vermiform appendix corresponded to the one just mentioned. The regional glands were all enlarged. Microscopical examination showed that the primary carcinoma had developed upon the base of a gastric ulcer. Upon examining the constriction nearest the ileocecal valve the circular thickening was found to be due to uniform infiltration with the tumor-cells, which did not involve the serous or mucous membrane. The serous membrane was simply drawn in, in that way causing

the constriction. The carcinoma cells extended through the muscular and submucous layers to the mucous membrane only; the muscular fibers were not involved. Only the lymph paths contained the cells, which were polygonal, from pressure. At no point were the cells found in the free lumen of the bowel, and the mucous membrane being everywhere intact, Brosch excluded contact-infection, reporting it as a case of "carcinomatous lymphadenitis" and "lymphangitis."

With these cases before us the microscopical study of our case of primary carcinoma of the pyloric end of the stomach, with secondary metastatic foci in the ileum, becomes quite interesting. Sections were made and stained in the ordinary way of the primary tumor, of a cross-section of the entire bowel where it was most thickened, of parts of the intestinal wall at the various constrictions and of the regional glands. The section from the primary tumor showed typical carcinomatous structure.

The cross-section of the bowel where it was most thickened showed under low power a marked peritonitis, with round-cell infiltration on the serous and subserous coat.

Examining from without inward we first notice the presence of carcinoma-cells just beneath the serous coat. The cells at this point are round. In the same area is a marked leucocytic infiltration. Passing toward the lumen of the bowel we find the number of carcinoma-cells gradually increasing until the mucous membrane is reached, where they are absent. The muscular layer is greatly thickened, and between the muscle-fibers the carcinoma-cells can be seen streaming towards the sub- the naked eye in the form of a faint blue line between mucous layer. This is so marked that it can be seen with the circular muscle-fibers, and from this at apparently regular intervals streaks of carcinoma-cells can be traced to the submucous membrane. Occasionally are seen large areas of cells packed closely together. Under high power these conditions are more easily made out.

By tracing out one of these blue streaks, composed of carcinoma-cells, it is seen that the cells pass between the muscle-fibers. The cells are round in the subserous coat, becoming spindle-shaped while passing through the narrow spaces, and becoming round again when the effects of pressure are removed in the submucous coat. The mucous membrane is intact and no carcinoma-cells are seen in the free lumen of the bowel. The blood-vessels are normal, containing only blood-corpuscles. The sections taken where perforations had occurred revealed similar structure, and in addition a marked necrosis, the different layers of the intestine being largely destroyed. The round cells are present in greater numbers, and there are a few nucleated round cells of large size. Some of the sections taken where the intestine is apparently normal to the naked eye showed occasionally in the submucous coat a few tumor-cells. The mesenteric lymphatic glands showed carcinomatous infiltration distinctly.

Conclusion.—As no tumor-cells are found in the free lumen, and the mucous membrane being everywhere intact, contact-infection can be excluded. The microscopical study of the specimens showed that a continuous growth in the wall of the digestive tract from the primary tumor to the metastatic foci had not occurred. The regional glands being involved, together with the retroperitoneal glands, the presence of carcinoma-cells in the lymph-vessels of the ileum not the result of immigration from the lumen or metastasis in the blood-vessels would seem to decide that this is another illustration of retrograde transportation of tumor-cells in the lymph-vessels. The perforations occurring at the same time would indicate the common cause and a common mode of origin. From the fact that they were found where the flexion of the bowel was most marked (see post-mortem report) and in the sulcus formed by the flexion, they might be considered to be the result

of a quite acute interference with the circulation at that point, causing necrosis.

February 14, 1898.

BIBLIOGRAPHY.

1. Virchow's Archiv, Bd. c, S. 503.
2. Ziegler's Beiträge, Bd. xviii.
3. Virchow's Archiv, Bd. xli, 1867, p. 535.
4. Deutsch. Arch. f. klin Med., Bd. lviii, 1896.

THE DIFFUSE INFILTRATING FORM OF CARCINOMA OF THE STOMACH.

LUDVIG HEKTOEN.

On presenting a specimen of diffuse carcinoma of the stomach to the John Hopkins Hospital Medical Society, Professor Welch[1] remarked that there are three diseases that may produce gross alteration in the stomach, indistinguishable from each other to the naked eye, viz., cirrhosis or fibroid thickening of the stomach, primary infiltrating carcinoma and secondary infiltrating carcinoma of the stomach. Orth[2] regards the majority of instances of contraction of the stomach as due to carcinomatous infiltration, and Welch looks upon a large number of the older cases in literature reported as cirrhosis of the stomach as diffuse carcinoma of this organ, because the diagnoses were not made by microscopic examination.

The first specimen of primary infiltrating carcinoma of the stomach, which I show here, is an example of a fibrous carcinoma, or scirrhus, occurring in a woman 45 years old, who had suffered some months with ascites, which required repeated tappings; there was also progressive emaciation, but never any prominent gastric symptoms. Post-mortem there was emaciation, brown atrophy of the heart and atrophy of the liver. The abdomen contained about 800 cubic centimeters of reddish fluid. The peritoneum was universally rough and thickened and there were firm adhesions between the intestinal coils and the external wall; between the adherent structures

[1] Bull. Johns Hopkins Hospital, October, 1893.
[2] Pathologische Anatomie.

cystic accumulations of clear fluid existed, especially about the cecum, around which the structures were matted together in a hopeless tangle. There were adhesions around the spleen, the stomach, and the pelvic organs. The omentum was drawn up into the form of a thick ridge across the upper part of the abdomen. In the mesentery were bands of thick tissue containing small islands of yellow color. There was marked induration and contracted adhesions about the portal vein, the wall of which seemed thick, the lumen reduced. There was no portal thrombosis.

On separating the perigastric adhesions, the stomach was found to be a small mass about one-third the size of the normal organ; it weighs 389 grams. It seems like a solid, hard organ and retains its outline in whatever position it is placed. Its serous surface is rough and shreddy, the serosa thickened, especially along the greater curvature, where the thickening extends into the contracted omentum; the induration and thickening ceases abruptly at the duodenal and esophageal limits.

Palpation does not indicate a hollow organ. An incision along the lesser curvature reveals a small balloon-shaped cavity, the bulb corresponding to the fundus: the cavity would probably hold 150 cubic centimeters. The mucosa is entirely smooth, pinkish, but thrown into huge stiff folds on account of great thickening in the submucosa. The duodenal and esophageal mucous membranes appear normal. The walls of the stomach are greatly thickened, mostly along the larger curvature: here the wall is 1.5 to 2 centimeters thick: the thickening is due to changes in the submucous and subserous coats principally: these are composed largely of a hard gristly substance. The muscular coat appears more hypertrophied. In no part of the stomach is there any primary tumor. There were no isolated metastases.

Microscopically it is shown that the thickening is due to the growth of a large amount of fibrous tissue in the submucous and subserous coats and to hypertrophy of the muscular layer. Shrunken epithelial cells are present in all coats arranged in small rows and alveolar masses, but the fibrous tissue predominates markedly, and it was necessary to make many sections in order to find any distinct carcinomatous structure. The mucous membrane is not at all characteristic because of a diffuse destruction of its cells and glands. Sections from the omental and peritoneal thickening also show a fibrous carcinomatous structure.

Here we have, then, a diffuse infiltrating fibrous carcinoma of the whole stomach: the growth is primary. The carcinoma has infiltrated the omentum, the peritoneum and the perigastric structures, result-

ing in great thickening and contracting dense adhesions which, among other results, led to compression of the portal vein and its branches, thus producing an ascites which is of interest from the standpoint of differential clinical diagnosis.

The second specimen of diffuse carcinoma of the stomach concerns an example of the somewhat rare form of infiltrating medullary carcinoma, the ulceration of the mucous surface being confined to a small circumscribed area.

The patient was a man 45 years old, in Dr. Edwards' ward in the Cook County Hospital. The following facts have been abstracted from the clinical notes. The illness began about four months before death with pain in epigastrium, vomiting of food only; has lost almost forty pounds in weight. He was much emaciated, the skin sallow and harsh. There was tenderness over the whole abdomen, the stomach apparently covered by the greatly enlarged liver, which reached below the navel and into the left hypochondrium, being somewhat dome-shaped. Three attempts to secure stomach contents failed; the tube seemed to meet some obstruction at or near the cardiac end of the stomach.

The post-mortem showed emaciation and general icterus. There were small but firm nodules on the peritoneum. The lymph glands in the hilum of the liver were much enlarged and caused pressure on the bile-ducts, the gall-bladder being greatly distended. The retrogastric and retroperitoneal lymph glands were also enlarged and infiltrated. The stomach is very small; it weighs 150 grams; the cavity is very materially reduced in size. On the posterior wall near the esophageal opening is an ulcer with raised margins and rough floor, about 2 by 3 centimeters in extent. Spreading apparently from this point, there has occurred a diffuse infiltration of the walls of the stomach leading to great thickening of all the coats of the organ, which gradually becomes less marked as the pylorus is approached, so that at a point about 6 centimeters from the pylorus the walls seem of normal thickness. The mucous membrane is covered with a grayish black mucus. The liver contained innumerable secondary tumors and weighed 5500 grams.

Microscopically (sections demonstrated) the tumor of the stomach is seen to be made up of rather small irregular epithelial cells arranged in a loose stroma in quite solid heaps and columns, which have grown diffusely throughout the coats of the stomach, following apparently the lymph vessels, the infiltration being most pronounced in the submucous and subserous coats, but invading the muscular coat also, in the form of a branching small-alveolated carcinomatous network.

April 11, 1898.

ON KOEPPE'S THEORY REGARDING THE FORMATION OF HYDROCHLORIC ACID IN THE STOMACH.

JOHN A. WESSNER.

Kœppe's theory that the formation of free hydrochloric acid in the stomach is the result of the ionization of NaCl in the stomach and of acid carbonates and phosphates in the blood whereby the H-ions in the blood are exchanged for the Na-ions in the stomach is a beautiful theory—on paper[1]. Koeppe has, however, failed to prove the correctness of the theory and the further investigation on the subject of which promises were held out in his first paper have not yet appeared.

The following experiments prove completely, as it seems to me, that Kœppe's theory is without foundation in fact. Fasting stomachs were first washed out with cold water to remove the greater part of the chlorides and the free HCl that is frequently found in fasting stomachs[2].

Turck's gyromele or revolving sound was then introduced and rotated for a few minutes. The stomach contents, perfectly neutral in reaction before the introduction of the gyromele, now gave very pronounced reaction with the reagents of Gunzberg and Boas, and by titration the acidity was found to correspond to 0.1 per cent. HCl.

Against this experiment may be advanced the objection that NaCl molecules first entered the stomach from the blood on stimulating the mucous membrane with the gyromele, and that this sodium chloride was thus ionized and converted into free HCl by the abovementioned exchange of Na and H-ions. This would be in harmony with Kœppe's assumption that NaCl molecules can pass through the mucous membrane, while the Cl atoms can not do so. Although this assumption of

Kœppe's is far from proven, the objections that could be made on the strength of it were met by the following experiment: After washing the stomach, physiological salt solution (0.7 NaCl) was introduced and allowed to remain for about ten minutes. If Kœppe's theory were correct, this salt solution should certainly have contained more or less free HCl. Not a trace could, however, be detected either by Gunzberg's or by Boas' reagents. By subsequent use of the gyromele, however, there was again obtained very strong HCl reactions and titrations again indicated an acidity of about 0.1 per cent. HCl.

From these experiments we must conclude that Kœppe's theory is untenable, and that the HCl of the stomach juice is a product of the cellular activity of the glands, whatever may be the chemistry of its formation. It may be added that the above experiments have repeatedly been carried out, not only on normal persons, but also on patients suffering from hyperacidity; yet in every case the result was the same. The production of hydrochloric acid was easily produced by means of the gyromele, but not by the cold salt solutions.

In conclusion, I wish to record three interesting cases of chronic gastritis upon which experiments similar to the above (omitting the salt solution) were performed. The stomach contents in these cases showed no trace of free HCl either before or after using Turck's gyromele. On estimating the total chlorides in the contents before and after evaporating to dryness on the waterbath (according to method for estimating free HCl there was, however, found a difference of about 0.1 per cent. of chlorine.

In one of these cases the stomach contents was found alkaline. The patient was given 20 drops three times daily of dilute hydrochloric acid U. S. P. At the end of two weeks an examination was made of stomach contents (on Ewald test meal). Reaction still alkaline.

but Boas and Gunzberg reagents gave a beautiful hydrochloric reaction. The experiment repeated next day gave the same result. A few days later an examination was made of stomach contents twelve hours after eating. Reaction alkaline. Boas and Gunzberg were again positive.

The total chlorine estimated before and after evaporation gave a difference of 0.1 per cent. of chlorine. Two weeks elapsed before patient was seen once more.

The contents on a test meal was now found distinctly acid; total free hydrochloric acid 0.2 per cent.

A few days later on examination on an empty stomach the contents still showed an alkaline reaction. Boas and Gunzberg, however, gave a good hydrochloric acid reaction[3].

The question that here naturally presents itself is in what form was this volatile chloride present in the gastric contents, and do the so-called hydrochloric acid secreting cells in reality secrete, not hydrochloric acid directly, but some compound of HCl which bears to the latter a relation like that of the zymogens to the enzymes? Investigations looking toward the clearing up of these points are being continued.

June 14, 1898.

BIBLIOGRAPHY.

1. Pflüger's Archiv, 1896, lxii, 589.

2. The washwater must be cold. Warm, even moderately warm water, has a sufficiently stimulating effect to produce quite perceptible traces of HCl. Cold water, on the other hand seems to paralyze the HCl secreting cells even in cases of hyperacidity and by means of such water the stomachs are quite readily washed free from hydrochloric acid. The chlorides, on the other hand, can not be completely washed away as I, in fact, observed in my first experiments on this subject. (Medicine, Chicago, 1895.)

3. During these experiments the patient did not take hydrochloric acid. Boas and Gunzberg reagents were freshly prepared and an evaporation gave no red color.

A REPORT OF TWO CASES OF GANGRENOUS PANCREATITIS WITH DISSEMINATED FAT NECROSIS.

HERMAN A. BRENNECKE.

While on the house staff of the Cook County Hospital two cases of gangrenous pancreatitis came under my observation. Although the knowledge of pancreatitis has greatly increased during the past few years instances of this interesting disease are still so infrequent that the following cases are deserving of report:

CASE I.—Susie L., age 47, white, married, Irish; was admitted to the service of Dr J. B. Murphy, June 7, 1897. Her father and one sister died of tuberculosis, the mother is still living and well. The patient is the mother of three children and has had two miscarriages. The last labor occurred twelve years ago and in all labors the puerperium was normal. The menses were always normal. She denied all syphilitic history. Her daughter informed us later that for the past nine years she had been drinking brandy to excess. The patient informed us that she had had "Bright's disease" for the past few years and had been in the "Sisters' Hospital" for the same. Otherwise her health had always been good. Her present illness began five days before entrance to the hospital. While going to market she was seized with severe cramps in the abdomen and "fell to the ground." She had to be carried home and was given morphin hypodermically repeatedly for the pain, which was severe enough to prevent sleep. At the onset she also had a chill and vomited several times. The bowels were constipated for the first five days. The sharp, piercing pains had recurred several times; they did not radiate in any particular direction and were located in the epigastric region.

Status praesens.—The patient is well nourished, the face flushed, the conjunctivæ subicteric; the pupils are equal and respond to light and accommodation. The nose and ears are negative: the pulse is rapid and weak (124); the chest is symmetric; the respirations are shallow and somewhat rapid (30); the lungs and heart are negative; the abdomen is distended, tympanic and very tender; in the right hypochondriac region there is an area of increased resistance. The tenderness, though general, is most marked in the epigastric region; no evidences of syphilis were found; an examination of the urine showed the following: acid, straw color, specific gravity 1012, slight amount of albumin, a few hyalin casts but no sugar.

During the course of her illness several examinations for sugar were made but none was found.

The patient would not consent to an operation until three days after her admission to the hospital. After the usual preparations for laparotomy had been made the patient was anesthetized with ether. A vertical incision about three inches long was made in the right hypochondriac region directly over the indurated area. The parietal peritoneum was sutured to the skin. The intestinal coils were found matted together by a fibrinous exudate. The omentum in this region was hyperemic, thickened and studded with small grayish areas; they were situated in the substance of the omentum and not raised above its surface; they varied in size from that of a pin head to that of a pea. The peritoneal cavity contained considerable clear, straw-yellow fluid. After walling off the peritoneal cavity with iodoform gauze a large gauze and rubber tube drain was inserted. A small piece of omentum was ligated off and excised for microscopic examination, which showed that the grayish areas were typic foci of fat necrosis, such as are seen almost without exception in cases of pancreatitis. The wound was dressed daily. After the operation the patient suffered less pain for a time. The dressings were always found saturated with a clear fluid. The borders of the necrotic tissue became rough and raised, and showed other signs of sloughing. The discharge soon contained shreds of fibrin and small masses of dirty gray necrotic tissue. The pulse remained at 120 to 130, the temperature varied between 100 and 102 and the respirations between 32 and 36. On the ninth day after admission she had an attack of sharp, cutting pains running from the lower end of the sternum to the back, which attack lasted about half an hour. At this time the facial expression was anxious, the tongue had a heavy white coat, the conjunctivæ were still subicteric, the heart and lungs negative. The pain in the abdomen had stopped, though the dirty gray discharge continued. The bowel movements were liquid, greenish-yellow and contained strings of mucus. Three weeks after the operation the patient was in about the same condition. The temperatures varied greatly between normal and 103. The pulse was weaker and more rapid (130 to 145); the respirations were rapid (40 to 48), but not costal in type such as are seen in acute peritonitis. After irrigating the wound for some time it would be noticed that considerable necrotic tissue still came from the upper angle. On exploration a large cavity was found below the right lobe of the liver which extended as far as the finger could reach toward the region of the head of the pancreas. Masses of loose necrotic tissue, which varied in size from a hazel to a hickory nut, could be taken from it with the forceps. The bowel movements and urination had become involuntary and the patient was very

restless. She had lost about ten to fifteen pounds in weight. Death occurred twenty-five days after the operation, with symptoms of a slow form of sepsis.

Autopsy, abstract.—Studding the omentum and to a lesser extent the parietal peritoneum, were numerous areas varying in size from those just visible to larger areas, 0.5 centimeter in diameter. Most of the areas, especially the larger ones, were surrounded by a narrow hyperemic zone. They were circular, white, well defined and not raised above the level of the surrounding tissue. Those in the parietal peritoneum were most numerous above the level of the umbilicus, but scattered foci were present here and there as low down as the brim of the true pelvis, on the serous coating of the psoas magnus and above the inguinal orifice. The intestinal coils were adherent to each other and to the omentum, but easily separated. A considerable quantity of bloody fluid was present in each side of the abdominal cavity.

The pericardial cavity contained a sanguinolent exudate; both pleural cavities contained a moderate amount of clear yellow fluid; the lungs contained a few small calcareous nodules in the apices; the heart weighed 275 grams and was flabby; endocardium, myocardium, valves and orifices showed no gross changes; there were no changes in the coronaries or intima of the ascending aorta; the spleen weighed 230 grams, large, soft and adherent to the under surface of the diaphragm; on section it showed a large white infarct the size of an English walnut; the kidneys were alike in appearance, external surfaces smooth, capsules readily removable, cortical markings fairly distinct and relations of pyramid to cortex normal; together they weighed 325 grams; the uterus was small and presented the changes commonly seen in chronic endometritis; the right Fallopian tube was dilated and contained a small quantity of purulent fluid; the liver weighed 1500 grams, was soft and light red in color; on section the lobular markings were distinct; the gall-bladder contained a thin pale bile, scanty as to quantity; the common duct was patent.

The pancreas was represented by a mass of gray, granular necrotic tissue, which was easily torn in removal. The necrosis had more of a liquefactive character in the region about the head and right half of the organ. The left half was studded with numerous larger and smaller grayish districts, which at various points fused together to form still larger conglomerate grayish or grayish-yellow masses. The material composing these areas was distinctly cheesy and soft and appeared at times to be formed in part at least of retained and inspissated pancreatic secretion. In and around the pancreas considerable chocolate-colored fluid containing masses of necrotic tissue was found. The stomach was inherent to the spleen. Behind it was found a cavity well walled off which contained a hemor-

rhageous semi-fluid material with masses of necrotic tissue in it. The intestines showed no important changes except those incident to the peritonitis. Examination of the cranial contents was not allowed.

Anatomic Diagnosis.—Gangrenous pancreatitis, with disseminated fat necrosis; localized suppurative peritonitis, with laparotomy fistula; diffuse fibrinous peritonitis; infarction of the spleen; hydrothorax; chronic apical tuberculosis; cloudy swelling of myocardium and kidneys. Microscopic examination of the areas of necrosis in the omentum and pancreas showed the usual changes found in such areas, viz.: a central district of granular non-staining tissue débris, surrounded by a more or less marked zone of densely accumulated leucocytes. There were no signs of tissue proliferation about any of the areas examined.

Case 2.—William F., age 43, white, widower, Irish; was admitted to the service of Dr. J. B. Herrick, Sept. 28, 1897. The family history is negative. The patient was a railroad man and drank daily fifteen to twenty glasses of whisky as well as considerable beer. His health has always been good with the exception of an occasional "bilious attack." He denied all venereal history. His present illness began one month ago after eating a few small apples and drinking several glasses of cold beer. A few hours later, while still in the saloon, he was seized with severe pains in the abdomen. He was given several doses of morphin hypodermically as well as hot drinks containing whisky. Following this he had no bowel movements for five days and vomited everything, even water, when taken by mouth. The vomitus was never fecal. The urine, he said, was scanty and of high color. At times he referred the pain to the epigastrium, but usually to the right and left iliac regions.

Status præsens.—The patient is a large muscular man, weighing about 250 pounds; the skin is moist and warm; the tongue is covered with a heavy, dirty, white coat; his mental condition is good; the chest is symmetric in form, the respirations rapid and shallow (28 to 36); no adventitious signs are revealed on examination of lungs; the respiratory excursion is somewhat thoracic in type; the area of cardiac dulness is slightly increased in all directions, no adventitous sounds heard; the pulse is rapid and feeble; the abdomen is much distended and the walls thick; there was dulness in the flanks and an area of dulness in the right iliac region.

Though he did not usually complain of pain, his abdomen was diffusely tender, most marked in the iliac fossæ; numerous pigmented scars were found over the tibial region. While under observation in the medical ward his pulse varied between 116 and 120 and was very weak; the temperature was usually normal, but at times would rise to 100 and 101 degrees F.; respi-

rations varied between 28 and 36. On several occasions he had attacks of severe prostration, characterized by the extremities becoming cold and cyanotic and his radial pulse growing almost imperceptible; at other times he would be restless and sleep but little. The vomiting was persistent; the only thing retained was whisky given in half-ounce quantities. Purgatives and repated colonic flushings failed to bring away any fecal matter. Six days after admission to the medical ward, though in a precarious condition, an operation was considered advisable and the patient was transferred to the surgical service of Dr. T. A. Davis.

An exploratory operation was decided upon and a vertical incision about three and a half inches in length was made in the right iliac region, where an area of dulness was outlined. As soon as the peritoneal cavity was opened a gray turbid fluid containing shreds of necrotic tissue and fibrin escaped. The omentum was much reddened and studded with white areas, pin head to pea size, which were not raised above the surface. The intestines and omentum were matted together by fibrinous adhesions, and walled-off numerous pockets containing the same turbid gray fluid above described were found. A large gauze drain was inserted and antiseptic dressings applied. The patient died soon after the operation. The diagnosis of pancreatitis was confirmed by the post-mortem findings.

Autopsy.—The post-mortem examination showed the following: A man, well nourished, neck thick, chest full, abdomen distended, rigor mortis well marked. In the right flank is a recent incision about four inches long, from which bloody fluid exudes. Slight adhesions exist between the abdominal wall and the omentum. The peritoneum is rough with fibrinous masses adherent to it. In the omental fat, and to a lesser extent the abdominal wall, are irregular grayish white patches varying from minute to larger coalesced areas. Those in the abdominal wall are found only near the peritoneum. The abdominal cavity contains a turbid grayish red fluid. The pleural cavities are empty. The pericardial cavity is empty and its surface smooth. The tongue, pharynx, trachea and esophagus show no changes. The thyroid is small. The lungs crepitate throughout and their lower lobes contain much frothy blood. The peribronchial glands are enlarged and markedly calcareous. The heart weighs 400 grams and on its anterior surface is an irregular white patch, at the lower border of which there is calcareous material. It contains fluid blood and a few large clots in the right side. The tricuspid orifice admits six fingers. The right auricle is large. The endocardium is normal with the exception of a few areas of thickening in the mitral valves. The mitral admits five finger tips. There are several aberrant chordæ tendinæ in the left ventricle. The heart muscle is smooth and flabby, reddish yellow in color.

and has a boiled appearance. The coronary arteries are tortuous and show a few yellow areas of thickening.

The spleen weighs 220 grams. Its surface is covered with a fibrinous exudate. It is soft, the pulp is swollen and there is little connective tissue. The kidneys together weigh 380 grams. The capsule is not adherent. The kidney substance is soft, the cortex swollen and the cortical markings indistinct. The urethra, bladder, ureters and testicles are negative. The liver weighs 2100 grams, and is adherent to the diaphragm, which is pushed up to the third rib on the right side and the fourth on the left. The liver substance cuts readily, the surface being rather granular, of a uniform red color, with small areas of a deeper red. The gall-bladder is distended with thick, viscid, dark green bile. The mucous membrane is smooth and velvety.

A large cavity is found in the region of the pancreas. It contains fluid of a dirty yellowish gray color, mixed with shreds of disintegrated material. The fluid has escaped into the abdominal cavity through a rupture whose margins are necrotic, and of a bluish gray color. Stretching across the cavity are remnants of the pancreas, much softened. The entire pancreas is involved in the cavity and contents. The fat tissue around the pancreas contains numerous white areas like those found in the omentum. The coils of small intestine are slightly adherent to each other by fibrinous masses. Large clots of fibrin are found in the posterior part of the abdomen.

Bacteriologic examination.—There was found in the blood from the heart, and in the spleen, liver, kidney, and in the necrotic areas in the subperitoneal fat, a bacillus corresponding to the cultural and other characteristics of the bacillus coli communis.

Anatomic diagnosis.—Gangrene of the pancreas; disseminated fat necrosis of omentum and subperitoneal fat; diffuse sero-fibrinous peritonitis; acute degeneration of the kidneys; cirrhosis of the liver; dilatation of the heart and degeneration of the myocardium; sclerosis of the coronary arteries; calcareous and caseous areas in the peribronchial lymph glands.

A histologic examination of the areas of fat necrosis showed practically the same conditions as those of Case 1.

The literature of pancreatitis has been so recently summarized by Simon Flexner[1] that only a few salient points will be mentioned here. According to Fitz[2], fat necrosis in the peritoneal cavity is infrequent in the suppurative and relatively frequent in the hemorrhagic and gangrenous forms of pancreatitis.

The first attempt to prove the relation between the

pancreas and areas of fat necrosis was made by Langerhans[3]. From his studies he concluded that fat necrosis was due to a decomposition of the fat molecule and a combination of the fatty acid with calcium salts present in the blood, to form a calcium soap. By injecting fresh pancreas pulp into the peritoneal fat tissue of a rabbit he produced a local inflammation with areas of fat necrosis.

Experiments by Dettmer, Hildebrand, Korte and Williams show, as previously asserted by Senn: 1, That the secretion of the pancreas can enter the peritoneal cavity without causing inflammation; 2, in a certain number of cases the free sterile pancreas or its secretion causes areas of necrosis; 3, the element of infection plays an insignificant part.

Dettmer found that pure trypsin caused a serohemorrhagic exudate into the peritoneal cavity, but did not set up fat necrosis. Hence it was concluded that in all probability the fat-splitting ferment was the active agent.

Flexner experimented on cats and dogs, ligating the veins coming from the pancreas, or one-half of the pancreas itself. By both methods he caused fat necrosis. The conclusions of Flexner are: 1, in the peritoneal fat necrosis the fat-splitting ferment is demonstrable at certain stages of the pathologic process; 2, it is most abundant in the early period and may entirely disappear later; 3, though it can not be said positively that steapsin is the direct cause of the necrosis of tissue, such an assumption is rendered most probable by its constant occurrence in the diseased areas, its absence from healthy fat, and the nature of the pathologic changes; 4, the escape of the pancreatic secretion into the peri- and para-pancreatic tissues is the origin of the necrosis, and this escape is facilitated chiefly by lesions of the pancreas and by disturbances in its circulation. Fat necrosis occur-

ring from other causes is not excluded. It is quite probable, Flexner thinks, that some are due to microbic agents.

Accidental findings in the post-mortems show that mild cases of fat necrosis occur which do not cause death. Balser[4], who first described fat necrcosis, found it present in five out of twenty-five post-mortem examinations. The areas were present in the intra-acinous tissue of the pancreas or the adjacent fat tissue. Since that time they have been found in many instances in which a gross disease of the pancreas was wanting. In such cases the areas were usually small. In Balser's cases the cause of death varied greatly, as is seen from the following enumeration: 1, Male, 52 years old, much emaciated, phthisis pulmonalis; 2, male, 42 years old, general anasarca, aortic regurgitation and stenosis; 3, male, 61 years old, carcinoma of stomach, peritoneum and omentum; 4, male, 48 years old, much emaciated, carcinoma of stomach; 5, male, 60 years old, emaciated, cirrhosis of liver.

The etiology of pancreatitis is not definitely known. Syphilis and an excessive use of alcohol are mentioned by most writers as the chief factors. Eichorst, Kœnig, Senn, Strümpell, Loomis, Osler, Ziemssen and Eulenburg speak of pancreatitis as sometimes following acute tuberculosis, typhoid, pyemia, septicemia and parotitis. The chief symptoms mentioned by all are: Sudden onset, with violent colicky pains in the epigastrium, vomiting, early collapse, constipation or diarrhea, with frequent fat in the stools and sugar in the urine.

In the cases reported by the writer there was a history of the excessive use of alcoholics in one and of alcoholism and syphilis in the other. Both cases had a sudden onset with severe colicky pains, by one referred to the epigastrium, by the other principally in the iliac fossæ. The first case had diarrhea and later in-

voluntary bowel movements. The second had obstinate constipation. Both vomited excessively.

The surgery of pancreatitis is not definite. Senn[5] speaks of making a lumbar incision for drainage after making an abdominal incision. Kœnig, however, thinks a diagnosis is seldom made before the rupture of the pancreas into the free abdominal cavity has taken place. Eichhorst claims a positive diagnosis is impossible.

June 4, 1898.

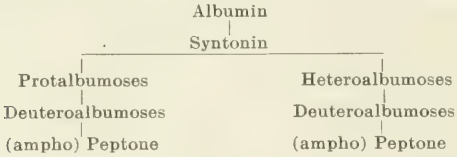
BIBLIOGRAPHY.

1. On the occurrence of fat-splitting ferment in peritoneal fat necrosis and the histology of these lesions, Jour. Amer. Ass'n of Phys., 1897.
2. Acute Pancreatitis; Middleton Goldsmith Lectures, 1889.
3. Experimenteller Beitrag zur Fettgewebsnecrose, Virchow's Festsschrift, 1891.
4. Virchow's Archiv. Bd. xc, s. 520, 1882.
5. Die Chirurgie des Pancreas gestützt auf Versuche und klinische Beobachtungen, Volkmann's Vorträge, No. 98.

ON THE PEPSIN DIGESTION—PRODUCTS OF PROTEINS.

OTTO FOLIN.

The men who are at present authority on the subject of the pepsin digestions and the albuminous splitting products produced by it are Professor Kühne in Heidelberg, and his two scholars, Professor Chittenden of Yale and Professor Neumeister at Jena. These investigators have, during the past fifteen years, exhaustively studied the products formed, and the results and conclusions found by them are generally accepted in the physiological chemical literature of the present. According to these authorities the pepsin digestion process is correctly represented by the diagram below which was first advanced by Neumeister and which is now more or less familiar to most of us:



According to this diagram the albumin is first converted into syntonin and the syntonin molecules are by the ferment split first into two different primary albumoses, the so-called protalbumoses and heteroalbumoses. These primary splitting products by the further action of the pepsin acid are converted into the secondary products which Kühne has called deuteroalbumoses. The deuteroalbumoses given by protalbumoses and those given by heteroalbumoses are not quite identical, but are so much so that no attempts have been made to separate them. The only reason for not considering the two perfectly identical is the observation of Neumeister's that if the primary prot- and hetero-albumoses be separated and each be subjected to further digestion, the secondary albumoses obtained from the heteroalbumoses will not be quantitatively precipitated by ammonium sulphate, while the deuteroalbumoses obtained from the protalbumoses are so perfectly precipitated that the biuret reaction can not be obtained in the filtrate.

By continued action of the pepsin acid the deuteroalbumoses are still further split and give as the final products of the pepsin digestion the "genuine" peptones.

Without attempting to go into an exhaustive review of the voluminous literature on the subject it may be well briefly to go over the reasons why the pepsin digestion is said to take place as indicated by the above diagram. It has long been known that acid alone gives syntonin or acid albumin. After adding pepsin in addition to the acid and digesting for a relatively short time, Kühne and Chittenden obtained by dialysis,

a product, the "heteroalbumoses," and by saturating the filtrate with sodium chloride they obtained another product, the "protalbumoses." That these two are the first formed or primary products Kühne and Chittenden proved, first by showing that they would get more of these and less of other splitting products after digesting but a short time, and that the conditions were reversed if they let the mixture digest a long time. The primary nature of the prot- and hetero-albumoses is with still greater certainty shown by the fact that if these two be isolated and then again subjected to pepsin digestion they disappear. No heteroalbumoses are now obtained by dialysis and no protalbumoses by saturating with sodium chloride. But by saturating the solutions with ammonium sulphate there is obtained in each case a product which seems to be practically identical whether the protalbumoses or the heteroalbumoses had been used as starting material for the digestion. This product which is precipitated on adding an excess of ammonium sulphate is the deuteroalbumoses, and since these are thus formed out of the primary albumoses they are naturally looked upon as the secondary digestion products so long as no other products intermediate between the primary and deuteroalbumoses have been found.

The deuteroalbumoses similarly give, according to the Kühne school, by still further digestion, as the third and final splitting product of pepsin digestion, "genuine peptone." This is not precipitated by dialysis, nor by sodium chloride, nor by ammonium sulphate, but is obtained in the last filtrate after removing all of the above albumoses.

To recapitulate, there are three different pepsin digestion products corresponding to three different stages in the digestion process, the primary albumoses, the secondary albumoses, and the peptones.

The chemistry of these products is interesting and

certainly important, but unfortunately we are as yet able to make scarcely any unimpeachable statements in regard to their chemical constitution, except that they are probably highly complex molecules which by chemical decomposition are broken down into certain well known amido-acids, leucin, tyrosin, asparagin, etc., and certain newly discovered bases of unknown constitution, arginin, histidin and lysin. The products have repeatedly been analyzed in the laboratories of Kühne, Chittenden, Neumeister and others, and by these analyses the remarkable fact has been brought out that they all have approximately the same percentage composition, namely in round figures:

C, 52 per cent.; H, 7 per cent.; O, 21 per cent.; N, 16.5 per cent.; S, 1.2 per cent.

These percentages of composition are also practically identical with the composition of undigested protein substances. Hence, if we were to depend on the analytical results alone we would conclude that the pepsin digestion does not chemically change the protein bodies. These analytical results are explained, however, by the assumption that the protein molecules have a constitution which can be correctly represented by the following algebraic formula: $(C_a, H_b, N_c, O_d, S_e)N$ in which case it is evident that the molecule could be split into as many smaller molecules as is represented by the algebraic term N outside the parenthesis. Each splitting product would then naturally contain the same percentage composition as the original undivided molecule, except for the small differences introduced by the addition of water in the process of the splitting. A similar condition does, in fact, exist in the case of such complex carbohydrates as starch, cellulose, or glycogen, all of which break down by proper treatment into the relatively small dextrose molecules without suffering and change in the percentage composition of the various intermediate products. The analogy of the carbo-

hydrate and protein splittings may be indicated by the following table:

Starch	$(C_6H_{10}O_5)_n N - H_2O$	Albumin	$(C_{72} H_{112} N_{18} O_{22} S_2)_n N$
Dextrines	$(C_6H_{10}O_5)_n N - H_2O$	Prim. albumoses	$(C_{72} H_{112} N_{18} O_{22} S_2)_n N'$
Maltose	$(C_6H_{10}O_5)_2 - H_2O$	Sec. albumoses	$(C_{72} H_{112} N_{18} O_{22} S_2)_n N''$
Dextrose	$C_6H_{10}O_5 - H_2O$	Peptones	$(C_{72} H_{112} N_{18} O_{22} S_2)_n N'''$

While presenting this analogy I wish, however, to make the following points of comment: 1. The carbohydrate series was known first, and this may naturally have led to the assumption that the protein molecules form a similar series without such rigid analytical proofs as exist in the case of the carbohydrate series. 2. It is not clear that the analogy exists, when we consider that the definite and well known unit in the carbohydrate series, the dextrose molecule, corresponds with the unit in the protein series, the "genuine peptone" which is in fact the least known of the protein splitting products and which, moreover, according to some investigators, does not exist at all (Pekelharing). 3. The theory has been constructed almost exclusively without taking the sulphur of protein molecules into account. 4. In my own investigations I have so far directed my analyses to sulphur alone and the results speak directly against the correctness of the theory. My own investigations along this subject were begun simply for the purpose of preparing some pure protalbumoses according to the Kühne-Chittenden method and without any intention whatever of entering this field of physiological chemistry either critically or otherwise. I did, however, not succeed by Kühne's method in getting out of ordinary pepsin digestion mixtures sufficient protalbumoses for the purpose on hand. This led me to try to find some other method. The well known fact that primary albumoses are precipitated by copper-sulphate from neutral solutions while neither secondary albumoses nor peptones are so precipitated was naturally thought of. Whether the older investigators ever tried to utilize this fact as a basis of separation is not shown

by the literature. The idea proved, however, to be a practical one and was soon developed into a method by which every trace of primary albumoses could be removed from any digestion mixture. By decomposing the copper-precipitate with hydrogen sulphate the albumoses were obtained free from copper. The experimental details of this work have been published in Hoppe Seyler's *Zeitschrift f. physiol. chemie.*, vol. xxv, p. 152.

Having thus readily obtained the protalbumoses the idea of also isolating the deuteroalbumoses and the peptones from their solutions naturally suggested itself. To obtain the deuteroalbumoses it was only necessary to remove the copper present in the filtrate from the protalbumoses by hydrogen sulphide and then to saturate this solution with ammonium sulphate, as is done by the old method. This also succeeded beyond expectation and gave about fifteen times as much deuteroalbumoses as can be obtained by first removing the primary albumoses according to the method of Kühne and Chittenden. The reason for this difference in the yield is that by the older method it is impossible to remove all the primary albumoses without also removing most of the deuteroalbumoses.

In regard to the final digestion products, the peptones, my results have, on the other hand, been negative, as were those of Pekelharing. I have found no genuine peptone in ordinary pepsin digestion mixtures, and have so far been unable even by the most persistent digestion of my deuteroalbumoses to convert them into genuine peptones.

In their chemical properties albumoses obtained by the above method of separation were found to be more or less different from the corresponding albumoses described by Kühne and his scholars. The behavior of the protalbumoses toward neutral lead acetate was most remarkable. By this reagent the protalbumoses of

Kühne are not precipitated, while the protalbumoses obtained by the copper salt method as above indicated is almost completely precipitated; similarly by acids, acetic, nitric, or carbonic, these albumoses are precipitated in the cold with the turbidity disappearing on heating. These facts do not agree with the properties of Kühne's protalbumose, and still his albumose should certainly have been found since the copper salt precipitated all of the primary albumoses present in the mixture. A search through the literature showed that the product which I had obtained as primary albumoses is such notwithstanding the fact that it is not included in the above diagramatical representation of the pepsin digestion process. Meissner obtained the same product some thirty years ago and describes it under the name of metapeptone as a regular primary, pepsin splitting product. Koch rediscovered the same substance in his tuberculin which is prepared from Witte's digestion mixture. Kühne verified Koch's description of the substance, while investigating the tuberculin, and later was able by Koch's method to obtain it directly from Witte's peptone mixture. Kühne pronounced the substance different from any previously known albumose and therefore gave it the name achrooalbumose. This name can, however, scarcely be accepted since Meissner had both described and named the substance twenty years earlier.

The product is a regular pepsin digestion product at least as important as the protalbumose of Kühne. Whether the substance be a primary or secondary splitting product of proteins, what its exact percentage composition, what its chemical and physiological properties may be—these are points to be cleared up and until this has been done we are justified in doubting the correctness of the current theory according to which the splitting process in the case of proteins is strictly analogous to the hydrolytic splitting of carbohydrates.

In regard to my secondary albumoses, those obtained by saturating the mother liquor with ammonium sulphate, I have also found some facts which are, theoretically at least, of considerable interest. The substances are certainly pure deuteroalbumoses according to the tests of Neumeister. Their behavior toward tannic acid, however, I found to be the same as the behavior shown according to Neumeister by genuine peptones alone in that they dissolve in an excess of the reagent. This fact proves either that the tannic acid reaction, contrary to Neumeister's statement, can not be used as a distinguishing mark between albumoses and genuine peptones or that the above albumose product and Neumeister's genuine peptone are identical substances.

The latter view which, in other words, means that pure so-called deuteroalbumoses are really final products of the pepsin digestion is in my opinion rendered more or less probable by the fact that I was unable to produce any further appreciable changes in my product by digesting it for six days with a very active pepsin-hydrochloric acid solution. Genuine peptone, according to Kühne, is a substance so hygroscopic that it hisses like phosphoric anhydride when thrown upon water. This statement of Kühne's has been very widely quoted throughout the albumose-peptone literature, but no one has, to my knowledge, verified the statement by actual experiment. In how far it may be literally true I must leave unsaid. The above albumose product after being digested for six days did not show any tendency to be hygroscopic after it had once been thoroughly freed from water by means of alcohol and ether, and it behaved in all other ways just like any of my other deuteroalbumose preparations, at least as far as I have yet been able to determine.

There is, however, one theoretically important point of difference between my deuteroalbumoses and the corresponding products of Kühne and Chittenden. Theirs

contain about the same percentage amount of sulphur as the undigested protein or about 1 per cent. My deuteroalbumoses average less than 0.3 per cent. Genuine peptone, according to Kühne's investigations, contain only about 0.5 per cent of sulphur, and because of this low percentage of sulphur genuine peptone has generally been supposed to be free from sulphur, the small amounts found being accounted for as impurity. If 0.5 per cent. sulphur can be considered as impurity in the case of genuine peptone then certainly can also 0.3 per cent. sulphur be so considered in the above deuteroalbumoses. But if a secondary digestion product of a protein contains no sulphur while the primary albumoses and the original proteins do, then it is clear that the splitting of proteins into primary and secondary albumoses can not be strictly analogous to the hydrolytic splitting of complex carbohydrates into simpler ones.

Aside from the theoretical considerations, this question of sulphur in protein digestion seems to me to be of some practical importance to the medical profession. It has been shown repeatedly that peptones and albumoses act as poisons when they are injected into the blood of an animal, while the same products will be absorbed and for a time at least utilized in the animal economy when taken as food. On the other hand, it has been shown that all peptone preparations are not equally poisonous when introduced into the blood and it has also been shown that no albumose or peptone product as yet investigated can take the place of undigested proteins for any considerable length of time. These facts, especially the last one, would be difficult to understand if in the formation of complex proteins out of smaller protein molecules there were an exact analogy to the formation of a complex carbohydrate like glycogen or starch from the simple sugars. But if on the other hand these digestion products differ in chemical compo-

sition and constitution then it is to be expected that different products will behave differently in the blood and it is then to be expected that selected, artificially prepared peptone preparations from which perhaps some very essential protein group, possibly a sulphur group, has been removed, can not be used to sustain a weak patient indefinitely even when absorbed through the digestive tract.

These investigations are being continued in the laboratory of Dr. Turck, according to a plan which we have worked out together.

October 10, 1898.

HEPATIC CIRRHOSIS IN THE GUINEA-PIG PRODUCED BY INOCULATION WITH A BACILLUS.

PRELIMINARY REPORT.

GEORGE H. WEAVER.

In view of the interest excited by the recent communications of Adami concerning a probable relation between bacteria and human hepatic cirrhosis, it seems desirable to make a brief report at this time of a bacterium that has come under my observation and that produces cirrhosis of the liver in guinea-pigs. The more detailed report will be reserved for later publication, when some of the details regarding the bacillus itself and the lesions produced by it have been more fully studied.

Adami[1] has found a bacillus in the cirrhotic liver of cattle affected with a localized enzoötic, known as Pictou cattle-disease. He demonstrated the presence of this organism in sections of the liver and adjacent lymph-glands, and obtained it in pure culture upon

artificial media. While the cultures, when inoculated into rabbits, guinea-pigs, and mice, caused death, the cirrhosis of the liver was not reproduced. From the liver in cases of human cirrhosis, Adami obtained cultures of bacilli that he places in the group of colon-bacillus. While he finds bacilli fairly numerous in the cells of the human liver, when death is due to various causes, he is able to demonstrate such bacteria in much larger numbers in the liver-cells and connective tissue in cases of cirrhosis. These bacilli he holds to be mostly dead, and he thinks they belong to the colon-group.

Cirrhosis of the liver has been observed in animals in the sequela of experimental injection of toxic materials. Flexner[2] has produced cirrhosis of the kidney and liver in rabbits by the injection of dog's serum into the circulation. In a rabbit dead 12 days after the injection, the microscopic appearances in the liver were an accurate reproduction of cirrhosis in man. In this liver there were present newly formed and forming connective tissue, proceeding from the portal spaces and also from the capsule, and irregularly distributed throughout the organ; numerous newly formed bile-ducts; and acute degenerative changes in the liver-substance, from which the sclerotic process distinctly started. In earlier cases (after 5 or 6 days) the liver showed areas of coagulation-necrosis. The leucocytes were not attracted to such areas of necrosis in such numbers as in cases of diphtheria or poisoning by abrin or ricin.

Focal necroses are observed in various infectious diseases, and it is quite possible for these necrotic areas to be replaced by connective tissue and a form of cirrhosis result. The cases of cirrhosis of the liver in children have been accounted for in this manner.

Reed[3] has recorded the case of a woman, 70 years of age, who died from carcinoma of the ovary, and who had passed through an attack of typhoid fever 25 years

previously. In the liver were found round, oval, and irregularly shaped areas of dense connective tissue, corresponding in their distribution to the areas of necrosis as observed in typhoid fever.

While foci of necrosis have been observed in the liver of animals after inoculation with pathogenic bacteria, the organism here described appears to be the only one studied that produces uniformly necrosis, rapidly followed by diffuse cirrhosis in the liver of the inoculated animal, and unaccompanied by marked changes in the other viscera.

I chanced to obtain this bacterium in following the routine practice of examining each animal that dies in our animal-room without previous inoculation. On September 22, 1898, a large female guinea-pig died without apparent cause, having been ill for two or three days. Upon examining the body the following conditions were found: A pneumonia involving one upper lobe, with a little reddish fluid in the pleura; punctiform hemorrhages beneath the pericardium near the apex; the liver pale and mottled grayish drab; the spleen large and dark red; the inguinal lymph-glands enlarged and red. Cover-slip preparations from the viscera disclosed the presence in the lung and spleen, and in smaller number in the liver, kidney, and blood from the heart, bacilli that did not stain by Gram's method. Cultures upon agar-agar plates yielded abundant colonies from the liver, spleen, kidney, lung and heart's blood. All the colonies were of the same bacillus.

The pure culture of the bacillus obtained from these plates, possesses the following characteristics. The bacilli are about the size of the bacillus typhosus, from two to three times as long as thick, usually single, occasionally in pairs end to end, non-motile and without flagella. They stain with the usual solutions of anilin dyes, in most instances uniformly, but occasionally more

deeply at the ends, especially with carbol-fuchsin. They do not stain by Gram's method.

Upon agar-plates, after 24 hours at 37° C., the deep colonies are the size of a pin-point, white and sharply outlined, and if slightly magnified they appear oval or round, sharply outlined and yellowish in color. The superficial colonies are white, opaque, sharply outlined, 2 mm. in diameter, slightly elevated, with a glistening surface. If magnified they appear round or oval, regular in form and sharply outlined, granular, of a yellowish color, and sometimes presenting radiating striations that pass toward the periphery where the colony becomes thinner.

Upon gelatin-plates 4 days old, the deep colonies are pin-head in size, and faintly yellowish white; when magnified slightly they are oval, sharply outlined and dark brown. The superficial colonies are from 2 to 3 mm. in diameter, white, elevated with finely-irregular edges; when magnified they are dark brown, granular, the edges being coarsely irregular with finer subserrations. Toward the edge the colony becomes thinner, usually gradually, and sometimes with more or less perfectly shown terraces.

On the slant of agar, the growth is abundant, white and confluent. On glycerin-agar the growth is similar to that on plain nutrient agar. On Löffler's solidified blood-serum the growth is abundant, elevated, and creamy white. On potato there is an abundant, elevated, spreading, faintly yellowish, creamy deposit, with gas-bubbles at times. Bouillon is first rendered cloudy, and later a clear fluid above is left by a settling of the bacilli to the bottom. In glucose-agar the production of gas is abundant. Litmus-milk is turned red after 24 hours at 37° C., and after 5 days it is decolorized and coagulated. In the puncture in gelatin a fine growth appears all along the track of the needle, with a thin surface-growth 1 cm. in diameter with a serrated border.

Grown on a slant of Kashida's medium (1½ per cent. agar, 1 per cent. urea, 2 per cent. lactose, colored with litmus) a white deposit forms on the surface, and the medium remains dark blue. If a similar slant after inoculation be placed in a jar containing pyrogallic acid and a 5 per cent. solution of potassium hydroxid, and the cover sealed, a white growth forms upon the surface, but the medium is turned red. A few hours after the tube is removed from the jar, the medium becomes blue again. The cultures have a slight aromatic odor. Indol is not produced on Dunham's peptone-solution, nor in bouillon prepared after Theobald Smith's method. The bacteria are killed by a temperature of 60° C. in 3 minutes, and by one of 70° C. in 1 minute, but not by one of 50° C. Carbolic acid in the proportion of 0.5 per cent. kills the bacilli within 24 hours, but weaker solutions have no effect.

The organs of the guinea-pig, after being fixed in alcohol, were cut and the sections stained in various ways for microscopic examination. The liver was the seat of extreme, diffuse fatty degeneration. In the solidified portion of the lung there was fibrinous exudate into the air-cells with blood. A large proportion of the air-cells were literally packed with bacilli. The kidneys showed no marked change.

The results of inoculation-experiments varied with the animal used, and the method and quantity of the culture employed. Inoculation with large quantities produced no effect upon rabbits, mice, pigeons, ground-squirrels and frogs. Guinea-pigs were killed by intraperitoneal, intrapleural and subcutaneous inoculation. From 0.5 to 1 cu. cm. of a 24-hours' bouillon incubator-culture, injected into the peritoneal cavity, killed guinea-pigs in from 8 to 20 hours. Under such conditions there was turbid fluid in the peritoneal cavity with varying quantities of fibrinous exudate upon the visceral serosa, sometimes there was none, and usually

but little. The liver and the kidneys were not altered macroscopically. The spleen was enlarged and firm; the adrenals injected; the pleuræ containing a little turbid fluid; the lungs were rich in blood, but without solidification. The left side of the heart was firmly contracted and empty; the right heart being dilated and filled with fluid blood. There was slight enlargement of the axillary and inguinal lymph-glands. Smear-preparations from the peritoneal and pleural fluids contained many bacilli, and in those from the blood and various viscera a few could be found. Plates from these various sources contained colonies of the inoculated bacillus in pure culture; from the peritoneal and pleural cavities in enormous numbers; from the liver, spleen, kidney, lung, gall-bladder, urine, and heart's blood in smaller numbers.

Microscopic examination of the tissues from these early cases showed slight desquamation of the glomerular and capsular epithileum, with granular material in the capsular space. The blood-vessels of the spleen were dilated and contained a varying number of large clear, uninuclear, phagocytic cells. In the liver there were zones of necrosis about the larger branches of the portal vein, with apparent increase of the lining endothelium. At times, there was beginning necrosis of the liver-cells adjacent to the prolongations of Glisson's capsule. Minute areas of necrosis of liver-cells with nuclear fragments were scattered throughout the liver. Occasionally phagocytic cells, similar to those in the splenic vessels, were observed in the vessels and capillaries of the liver. Guinea-pigs that were inoculated into the peritoneal cavity with a small amount of a bouillon-culture, or subcutaneously with 0.5 cu. cm. of a 24-hours' bouillon incubator-culture, lost weight and died after 8 or 9 days. Under such conditions the bacteria may have disappeared entirely before death, as cultures from the viscera failed to yield colonies. After

subcutaneous inoculation the bacilli were found only in the small abscess in the abdominal wall at the site of inoculation. The number of such experiments has been limited and wider variations may occur. After death the changes recognizable by the unaided eye are usually a pale, firm liver, which may feel slightly uneven upon its surface, a slightly enlarged spleen, edematous lungs containing much blood, a firmly contracted and empty left heart and a dilated right heart containing fluid blood. Under the microscope the spleen shows dilated sinuses, containing numerous phagocytic cells, enclosing blood-pigments and nuclear fragments. In the liver the changes are those characteristic of cirrhosis in this organ; marked proliferation of the bile-ducts; accumulation of connective tissue between the lobules and invading them; and necrosis of the liver-cells. The proliferating connective tissue seems to replace the areas of necrotic tissue seen in the earlier stages. Intraperitoneal injection of bouillon-cultures devitalized by heat produced after 9 days lesions similar to those just described. Injection into the peritoneal cavity of a bouillon-culture from which the bacteria had been removed by passing through a Chamberland filter, caused death, but without any apparent change in the viscera. The last two experiments were performed but once.

From the foregoing findings it appears that the bacillus described causes, as its chief effect, when inoculated into guinea-pigs, necrosis of the liver, and if death is sufficiently delayed, marked cirrhosis of the liver. The dead bacilli, in cultures devitalized by heat, produce the same effect as living bacilli if introduced into the peritoneum, but cultures from which the bacilli have been removed do not cause the changes in the liver that occur under other conditions. It is not certain how this organism should be classified, but so far as it has been studied it appears to possess more of the

characteristics of the members of the colon-group than of those of any other.

December 12, 1898.

1. Montreal Medical Journal, July, 1898; British Medical Journal, Oct. 22, 1898.
2. Transactions of the Pathological Society of Philadelphia, 1896.
3. Johns Hopkins Hospital Reports, v., 1895.

DISCUSSION.

DR. HEKTOEN.—Dr. Weaver's interesting observations in regard to the actions of his bacillus upon the liver are in a measure duplicated in the case of a bacillus which I have recently had the opportunity to study. Isolated from the surfaces of the lesions of a blastomycetic dermatitis, this bacillus corresponds morphologically and culturally to the bacilli of the pseudo-diphtheria group. On subcutaneous inoculation in guinea-pigs, rabbits, white rats and dogs it produces a marked infiltration, followed in some cases by necrosis and ulceration; the animals, especially guinea-pigs, die in from 3 to 6 weeks greatly emaciated; the livers show a more or less extensive recent proliferation of the connective tissue, producing a picture strikingly like that of various stages of ordinary human cirrhosis both macroscopically and microscopically; in the earlier cases there are present smaller and larger districts of necrosis in the livers around which the proliferation is especially pronounced. Diphtheria antitoxin does not protect the animals against the action of this bacillus.

A CASE OF AMEBIC DYSENTERY.

WITH REFERENCE TO PRIMARY CHANGES FOUND IN THE MUCOSA AND MUSCULARIS MUCOSÆ, AND WITH AN IMPROVED METHOD OF STAINING THE AMEBÆ IN THE TISSUES.

I. B. DIAMOND.

Patient F. W., a negro about 60 years of age, from whom a satisfactory history could not be obtained, was admitted to the Grady Hospital, Atlanta, Ga., October, 1896. He stated that his illness began with pain and looseness of the bowels seven or eight months prior to his admission. At that time he had from 5 to 10 actions daily; later the stools became bloody and changed to mucus. Since then he gradually became worse, with loss of flesh and strength, so that he was unable to

do any work. Occasionally has had attacks of nausea and vomiting. On admission he was considerably emaciated; temperature 97 F.; pulse 120 per minute; tongue slightly coated; loss of appetite; the abdomen somewhat distended and tender on palpation. The feces consisted of considerable mucus and blood, and gave off a peculiarly offensive odor. On microscopic examination, many active amœbæ, red blood-cells, pus cells and large epithelioid cells were found. He improved but little under treatment, gradually sank, and died on Oct. 22, 1896.

Necropsy, 12 hours after death. The body greatly emaciated; rigidity slight; abdomen somewhat distended. On opening the peritoneal cavity, the omentum found rolled up around the large intestines; serous surfaces moist; appendix normal. The large intestines fully distended and their walls greatly thickened, the thickening being most marked near the splenic flexure where the colon was bound down by very firm adhesions. On separating the adhesions a perforation was found in the colon near the splenic flexure. The opening was somewhat irregular and about one inch in diameter. On laying open the colon beyond this point, toward the rectum, the mucous membrane was found considerably ulcerated. These ulcers were of various size and shape, usually round or oval, and not larger than two inches in diameter; others not more than two or three lines in diameter. The floor and edges of the ulcers were unusually smooth. In others the ulceration extended below the mucosa, with some undermining of the edges. The mucous membrane from the point of perforation toward the cecum, was found extensively ulcerated, more in patches, irregular and with ragged edges and walls. The remaining mucosa was greatly congested, and apparently hemorrhagic at many points. In the ileum near the ileo-cecal valve many ulcers were found, resembling those described in the colon. The ileo-cecal opening was considerably contracted, due to an increased thickening of the fibrous tissue around the orifice. The *mesenteric* glands were swollen. The *spleen* was normal in size and in appearance. The *liver* was somewhat enlarged and congested. On section pale areas, the size of a pin's head, could be seen scattered throughout its substance. Both *kidneys* were larger than normal. The capsules somewhat adherent and substance pale. Bladder normal. The heart, lungs and other organs normal.

Pieces of the various tissues were fixed in the Haidenhein corrosive sublimate salt solution, hardened in alcohol and embedded in paraffin. Effort was first made to stain the amebæ in the tissues as recommended by Harris[1], namely: with toluidin blue. By this stain the

[1] Harris: Amebic Dysentery; Am. Jour. of the Med. Sci., April, 1898.

amebæ are brought out prominently, and can be easily distinguished from other objects, especially the large round degenerated connective tissue cells which resemble the amebæ. I did not succeed, however, in staining them. The toluidin blue was quickly washed out by the alcohol, the amebæ and nuclei of cells either remained colorless or were stained by the diffuse stain, when counterstained. I then began to experiment with various staining solutions in combination with toluidin blue, in the hope that a combination might be found which would resist the alcohol used in the subsequent washing. I found that after mixing toluidin blue and carbol fuchsin together, a beautiful contrast stain was thus produced, the amebæ staining a purplish blue color, the nuclei of cells either blue, purplish blue or red, and the rest of the tissues, light to purple-red. The tissue should remain in the stain for ten minutes to several hours. It is then washed in alcohol and cleared in xylol. The internal structures of the amebæ are beautifully shown when the washing with the alcohol is a little prolonged. The vacuoles become quite distinct, and apparently surrounded by small granules reddish or pinkish in color. If the toluidin blue is in excess, the tissues and the amebæ are then stained more of a blue. This stain keeps well and does not deteriorate. It is made as follows: Toluidin-blue saturated aqueous solution, 1 part, carbol-fuchsin (tubercle stain) 1 part, mix, filter. This combination acts quickly, bears washing, is delicate, and gives the effect of a double stain. A somewhat similar result is obtained when the tissues are stained in carbolic acid toluidin blue, and counter-stained with eosin. Harris[2], in a recent article recommends this stain for general histologic work. He states it acts quickly, stains deeply and will bear any amount of washing with alcohol. He believes that the reaction if not acid, is certainly neutral. This

[2] Phila. Med. Journal, May 14, 1898.

leads me to believe that the success I obtained in staining the amebæ in the tissues, is due to the carbolic acid in the staining solution, besides helping to differentiate delicately the internal structures of the amebæ.

Morbid histology.—Intestine. Characteristic lesions of the intestine, such as those described by Councilman[3] and Harris, namely: "great swelling, infiltration and breaking down of the submucosa, with caving in of the normal mucosa above" were markedly absent. The changes here observed were largely confined to the mucosa and muscularis mucosa, any deeper ulceration being apparently secondary. The earliest changes show that the mucosa at the point which forms the beginning of the ulcer has become transformed into a peculiar homogeneous granular mass, which gradually softens and breaks down at the surface, while the mucosa near the seat of the degeneration is seen infiltrated with small round cells, which may even extend through the muscularis into the submucosa. The blood-vessels are dilated and filled with blood. Amebæ are occasionally seen near the surface of the mucosa, but usually they are deeper, and especially along the margin of the muscularis. This layer also shows marked changes. The nuclei have disappeared and the fibers at the seat of the ulceration are granular. Beyond this point it seems that the muscularis has undergone a kind of hyaline transformation. Many amebæ are seen in this layer, lying between the fibers which are swollen and separated from one another. In these sections, the ulceration rarely extends any deeper than the submucosa.

In the submucosa there is a decided increase of fibrous tissue. The walls of the blood-vessels in this layer are greatly thickened, with thrombosis and in some obliterating endarteritis. Large swollen connective tissue cells are not present. The enormous

[3] Councilman and Lafleur: John Hopkins Hospital Reports, vol. ii.

thickening of the gut at many points is due to newly formed fibrous tissue in the submucosa and outer layers, as is shown in many of the sections. There are also present in many of these sections, besides ulceration of the mucosa and muscularis spoken of above, secondary ulceration in the submucosa, which in some instances is quite extensive, reaching through the inner muscular tunic to the serous coat. The swelling is slight, but the small round cell infiltration is more pronounced with a tendency of slightly undermining of the mucosa.

Many amebæ are seen near the ulceration and among the small round cells. The products slowly break down, transforming the tissue into a homogeneous hyaline or granular mass, which forms the base of the ulcer, and in which a few cells and amebæ are still present. Large numbers of amebæ are found in all the coats. In many of the sections they are seen in the act of passing through the newly formed fibrous tissue and various layers into the outer muscular layer and thickened serous coat, producing but little if any change, a fact noted by Harris. The resistancy of this new tissue to the action or products of the amebæ is well observed even in the submucosa where the ulceration is slow and there is not that softening and breaking down of the tissue, observed in the mucosa. In many of the sections, for example, those taken from the irregular ulcerated and hemorrhagic patches of the transverse colon, the ulceration seems to be more of a pronounced kind. The ulceration not only involves the mucosa and muscularis mucosa, but the submucosa may be attacked quite early.

All the layers may be necrotic, and shreds of the various tissues hanging or lying over the ulcer; part of the submucosa or inner muscular layer may form the base of the ulcer. The blood-vessels, which have been reached by the ulceration, are broken down, or infiltrated with small round cells. Many amebæ are seen in the

walls as well as in the lumen of the vessels. *Sections* of the *liver* show a necrosis of the liver cells around the central veins; the latter are dilated and filled with blood. Amebæ are not present. The *mesenteric* glands show an increased number of lymphocytes, the lymph sinuses are dilated and contain many large swollen vacuolated cells which resemble the amebæ. The reticula of the glands are somewhat thickened, the blood-vessels dilated and congested. Sections of the *kidney* show cloudy swelling of the cells lining the convoluted tubules and those lining the glomeruli; the connective tissue seems somewhat thickened.

The points here of interest are of course the peculiar character of the lesions in the intestine. Councilman states that the amebæ do not at first produce any changes in the mucosa or muscularis, but pass through these layers into the submucosa and then produce the highly characteristic lesions, which always accompany their presence, namely: great swelling, infiltration and breaking down of this layer with undermining of the mucosa above until it caves in due to loss of substance below. Harris, on the other hand, describes a form of lesion in the mucosa which softens and breaks down at the surface, and that any deeper ulceration—in the submucosa—being apparently secondary. In these sections he also found the submucosa rather increased by new formed fibrous tissue below the ulceration. But he states he never found any amebæ in these ulcers.

That changes may first begin in the mucosa and muscularis mucosa is in this case well illustrated. Not only are the amebæ present in these layers, but the changes produced by them, can at the same time be accurately observed. Why the changes are confined in some instances in the mucosa and in others in the submucosa, can be undoubtedly explained to the resistance of the tissues, when in a healthy state.

A CONTRIBUTION TO THE PATHOLOGY OF CHRONIC, HYPERPLASTIC TUBERCULOSIS OF THE CECUM.

BASED UPON THE STUDY OF TWO CASES, IN ONE OF WHICH CARCINOMA OF THE CECUM COEXISTED.

T. R. CROWDER.

As early as 1835 a case of tuberculosis of the cecum is recorded by A. Dupin. Valy in 1843 and Bodard in 1844 recorded cases of tuberculous typhlitis, and Leudet in 1859, basing his conclusions upon extensive investigations, placed the so-called "typhlitis stercoralis" in the class of tuberculous affections of the cecum. In these earlier reports, however, no particular distinction is drawn between acute and chronic or between localized and progressive forms of tuberculosis of the intestinal tract.

On account of its usual association with tuberculosis of the lung so extensive as to contraindicate operative procedures, its rapidly spreading character and its frequent extensiveness before clinically recognized, intestinal tuberculosis belongs chiefly in the field of internal medicine. The great development in the application of surgical treatment to all sorts of localized intestinal lesions during the last decade and the progress in surgical pathology have, however, called attention to a form of circumscribed, long localized tuberculosis of the bowel, which may be successfully treated by operative methods. This hyperplastic form of tuberculosis has its counterpart in certain cases described in which the disease has been located in the skin, larynx, and joints and certain cases of so-called Hodgkin's disease which have proven post-mortem to be of a tuberculous nature but to have given rise to fibrous hyperplasia rather than to caseation and destruction of tissue. The

condition is characterized pathologically by a great thickening of the bowel wall and a narrowing of its lumen. The hyperplasia of the coats of the intestine gives rise clinically to a tumor formation many times resembling a carcinoma.

This form of intestinal tuberculosis is met with most frequently in the region of the cecum. According to Conrath[1] its pathological anatomy was first described by Durante at the seventh Italian Surgical Congress in Florence in 1890. At a meeting of the Gesellschaft der Wiener Aertzte in 1891 Billroth[2] demonstrated a resected cecum which had presented itself clinically as a large hard swelling in the right iliac region, in every respect resembling a carcinoma. He called attention to the clinical similarity of the two conditions and to the difficulty of making a differential diagnosis even when the tumor is removed and subjected to a careful macroscopic examination. He expressed the opinion at that time that tuberculosis does not always result in destruction of tissue and that the epithelioid cells may become fibrous, resulting in the formation of a firm tumor.

Hartman and Pilliet[3] before La Société Anatomique de Paris in 1891 called attention to a form of tuberculous typhlitis which accurately resembles a carcinoma and which is not to be distinguished from it by the naked eye. They also expressed the opinion that a large number of cases published as carcinoma and lymphosarcoma were in reality tuberculous affections of this nature.

In 1892 Sachs[4] was able to collect twelve cases from the literature to which he added a very typical one successfully operated upon by himself. In this case there was a tumor the size of an orange located in the cecal wall and almost obliterating the bowel lumen. There was no caseation of the retrocecal lymphatic glands and no ulceration of the intestinal mucosa. The tumor

was nodular and uneven and was considered carcinomatous until the microscopic examination revealed its true nature.

Presenting a case before La Société Anatomique de Paris in 1894 Pilliet and Thierry[5] characterize chronic tuberculosis of the cecum by three things: 1. Anatomico-pathological; there is a great thickening of the wall of the cecum in the region invaded and especially of the mucosa, which at the borders of the ulcers mounts into knob-like outgrowths. 2. Clinical, and depending upon the first; the formation of a tumor. 3. Therapeutic; it remains long localized and all the part of the intestine invaded may be resected with success, thus benefiting the patient for a longer or shorter time.

Further contributions to the literature of the subject have been made by Czerny[6], Salzer[7], Hofmeister[8] König[9], Courtillier[10], Benoit[11], Conrath[1], Caussade and Charrier[12] and others. Perhaps the most thorough review of the subject in all its relations and especially from the surgical standpoint, is the article by Conrath. He was able to collect from the literature, personal communications and his own experience a total of 85 cases undergoing surgical treatment with a mortality of 16.7 per cent.

Development of a knowledge of the subject is largely due to the efforts of the French and German surgeons. It is a noteworthy fact that Conrath in his collection of 85 cases in 1898 cites but one from the American medical literature, that one by Dr. Beck[13] of Chicago. From the literature of this country I have been able to add but two cases to this number, these by Dr. Ochsner[14] and Dr. Senn[15] of Chicago. All three of these cases have been presented in a more or less extensive group of cases reported from a surgical point of view without summary of the general pathology of the condition.

In the literature of England I have found but two cases. They are reported by Page[16] and by Lediard[17].

The case by Page is stated not to be definitely tuberculous but to show a high degree of chronic inflammation of the cecum with hypertrophy of its wall and caseation of the retro-cecal lymphatic glands with the microscopic findings of tuberculosis.

That this form of cecum tuberculosis is sufficiently rare or sufficiently unknown to be deserving of further comment is shown by the fact that no direct reference is made to it in text books on pathology by Orth[18], Zeigler[19] and Birch-Hirschfeld[20], and is no more than mentioned by König[21] in the latest edition of his text-book of surgery, where he gives a very brief summary of the article by Conrath[1].

CASE 1.[22]—*Tumor-like tuberculosis of cecum; resection; end-to-end anastomosis; recovery.*

History.—A colored schoolgirl, 14 years of age, was admitted to Cook County Hospital, Aug. 15, 1898, and assigned to the service of Dr. E. L. Morehead. The following history was obtained upon admission: She comes of healthy parents; her father is living and well; her mother died in childbirth. It is said that she did not have phthisis. No specific history in either parent. One maternal uncle has scrofula and one maternal aunt died of pulmonary tuberculosis. A brother died at nine months and a sister at four years of acute diseases and a brother died at seven years of "quick consumption." No brothers or sisters living. The patient has had the ordinary acute diseases of childhood but has been otherwise always well. Has never menstruated.

The present trouble began about eight months ago with cramp-like pains in the abdomen. These were of a recurrent and somewhat periodic nature, at first slight and infrequent, gradually increasing in frequency and severity. They were at first diffuse but always referred themselves ultimately to the right iliac region. They would last ten or fifteen minutes, repeating themselves several times during each attack at varying intervals of some minutes. During the later part of last winter they were frequently accompanied by vomiting and came on three or four times a week to once or more daily. For the past three or four months visible, local, transitory swellings, accompanied by rumbling, have been noticed by the patient in the abdomen, coming on and disappearing with the pains. During the past two weeks the pain has been almost constant, always being ultimately referred to the right iliac region and accompanied by much vomiting. Bowels regular at all times

but appetite very poor. Only liquid food can be retained. Has lost much flesh.

Examination.—General nourishment poor; skin smooth and moist; eyes negative; tongue lightly coated; mucous membranes anemic; teeth well formed and regular. The chest is fairly well developed and respiratory movements free. The heart and lungs are negative. On inspection the abdomen shows localized distension of intestinal coils which change position as peristalsis proceeds. This action is easily palpable and gurgling, rushing sounds accompany it. There is tenderness over the whole lower abdomen, most marked in the right iliac region with point of greatest tenderness half way between the umbilicus and the anterior superior spine of the ileum. Lying deep in the abdomen upward and outward from this point is a firm, tender, smooth mass the size of a large lemon. This can be fairly well outlined by the fingers, is very slightly movable, is not affected by deep inspiration and is apparently free from the anterior abdominal wall. No lobulation or other unevenness of the surface can be made out. The external genitalia are negative; hymen intact and no vaginal examination made. The inguinal, axillary cervical and epitrochlear lymph glands are palpable but not large. Pulse 88, strong and regular; temperature 100 F.; respiration 24. Urine: sp. gr. 1032; reaction acid; no albumen or sugar.

Operation.—The patient was operated the morning after admission under chloroform anesthesia. An incision 3½ inches long was made in the direction of the fibers of the external oblique and bisecting a line joining the umbilicus and the right anterior superior spine. No adhesions were found to the anterior abdominal wall. Abdominal exploration reveals a firm mass, as described in the external examination, occupying the ileocecal region. It is but slightly movable and is brought forward into the wound with considerable difficulty after loosening firm adhesions posteriorly. It is found to be a slightly lobulated tumor mass involving the entire circumference of the bowel at the ileocecal junction. The lower ileum is dilated and the walls are thickened and somewhat indurated. The peritoneum is free from adhesions and is for the most part smooth, but for a distance of about an inch above the tumor shows a number of slightly roughened and depressed round and oval spots of yellowish white color measuring in diameter from one to five millimeters. The lymphatic glands lying in the mesentery next to the cecum are firm, white and considerably swollen. No vermiform appendix is recognized. A strong fibrous band passes from the caput cæci to the pelvic fascia at the pelvic brim and by traction exposes the right tube and ovary. This is ligated with catgut and divided. It is a solid fibrous cord without a lumen. The tumor mass including about two inches of bowel on each side was excised as rapidly

as possible—the patient's general condition becoming very poor—and, the colon and ileum being of practically the same size, an end-to-end anastomosis was made by a single row of Lembert sutures of fine silk. The parts were carefully dried, hemostasis assured and the bowel dropped back into the abdomen. A drain consisting of several strands of iodoform gauze was passed down to the sutured bowel ends and the external wound closed by a single row of silk-worm gut sutures embracing the whole thickness of the abdominal wall. The upper one of these, where the drain emerged, was left untied. About 600 c.c. of normal salt solution was injected slowly under the pectoralis major muscle during the latter part of the operation. The patient left the table with a very weak pulse of 156, respiration of 16 and warm dry skin. Nothing was allowed the patient by mouth except occasional teaspoonfuls of warm water during the first four days, water and liquid foods with whisky being administered by the rectum. She suffered very little from thirst or other discomforts and aside from a rise of temperature to 102.4 F. late on the day of operation made an uneventful and perfect recovery. The large drain was removed on the second day and a small strand of iodoform gauze inserted just through the abdominal wall. This was left undisturbed until the fifth day, when it was removed and the remaining suture tied. The wound healed throughout without suppuration. At the end of three weeks the patient left her bed and after another week left the hospital much improved in general health and flesh and without pain or discomfort in the abdomen. Seen during the latter part of December she had gained greatly in flesh and no evidence of tuberculosis could be found in the lungs or elsewhere upon careful physical examination.

Pathological examination.—The growth is situated in the wall of the cecum and involves its entire circumference. It begins above at what appears to be the ileo-cecal junction and involves about three inches of the length of the bowel, this distance being somewhat less on the mesenteric side. The surface is indistinctly lobulated and shows torn adhesions posteriorly. The wall is firm and resisting to the knife, whitish on the cut surface, with irregular yellowish areas and measures in thickness from 1 to 2.5 cm. The thickest part of the wall, which lies opposite the mesenteric attachment, shows in the center and just beneath the mucosa several pea-sized somewhat softened areas from which can be turned out firmer masses which lie loosely adherent and which appear to be necrotic. The original contour of the cecum is lost; it is as if the ileum and colon were joined end-to-end and a new growth occupied the wall at their junction. The lumen of the bowel included in the growth is somewhat funnel-shaped with the apex toward the ileum where it is scarcely as large as an ordinary lead

pencil. The mucous membrane is covered with thickly set little polypi, of an average size of large wheat grains, some of which are sessile and some of which have short pedicles. Some of these have branched extremities. They serve to almost entirely obliterate the remaining lumen. There is at no place any visible loss of mucous membrane. The lower ileum is nearly 5 cm. in diameter with greatly thickened muscular walls, measuring 4 mm. in places and very firm and inelastic. Situated in it are yellowish areas of firm fatty tissue. The mucous membrane is smooth and free from folds, but is congested and shows a few ecchymotic areas. The serous coat also shows a few ecchymotic areas and the roughened spots before described. At a point on the mucous membrane of the ileum exactly opposite the mesenteric attachment and about 5 cm. above the tumor is a polypoid growth the size of a small pea, slightly flattened, resting on a short pedicle resembling the polypi in the cecum. The wall and the mucous membrane of the colon beyond the growth are free from changes. Lying within the excised mesentery are four lymphatic glands the size of large hazelnuts, of moderate firmness, smooth and clear white on the cut surface. They show no areas of caseation or of softening.

Microscopical examination.—The greater part of the tumor is made up of a hypertrophied muscular wall showing a great increase in both the fibrous and muscular elements and containing more connective tissue cells than normal. The yellowish areas are ordinary adipose. There are many typical microscopic tubercles which are so closely grouped in some places that as many as ten may be seen in a single field (Zeiss obj. AA and oc. 3). They are most numerous in the submucous tissue, in places lying just at the basement membrane, but are of very irregular arrangement and not seen in typical form in all sections. The whole of the submucous tissue is densely infiltrated with deeply staining small round cells. Tubercles are found in the muscular coat in only a few places where a large confluent mass lies deeply imbedded in its center. The papillomatous mucous membrane shows great hyperplasia of the glandular elements after the manner of a benign papilloma with dense round-celled infiltration of the stroma. The epithelial cells are large, cylindrical and show all stages of mucoid degeneration. Over some small areas the epithelial covering is entirely lost and its place taken by an avascular granulation tissue. The epithelial tissue does not end abruptly where this granulation surface begins but shades gradually into it without any depression or unevenness. Glandular elements are found in places situated rather deeply in the wall but everywhere maintain a typical structure. Many of the gland lumina are greatly distended. Sections taken in proper directions through the part containing what were described as free bodies show

them to be large buried papillæ containing but a mere remnant of epithelial covering, lying within cavities showing likewise a mere remnant of epithelial lining, as if a large papilla during the process of its development had been bound to the serosa and the muscular and submucous tissue at its base had not undergone the general hyperplasia of that surrounding it. At the attached base of these papillæ is where is found the greatest infiltration of the deeper parts of the wall with tubercles. The more actively proliferating tissue surrounding them has entirely closed over them on the side toward the lumen, thus burying them completely. They show a central necrosis surrounded by an almost avascular granulation tissue containing giant cells. The field of mucosa and submucosa surrounding them shows a dense round-celled infiltration and contains an occasional giant cell.

The lymphatic glands of the mesentery contain a large number of microscopic tubercles in every way typical. Some of them show a beginning necrosis in the center but at no place is there found complete necrosis with caseation. These tubercles lie singly and in large confluent groups.

It was only after a long and painstaking search that tubercle bacilli were demonstrated either in the lymphatic glands or in the tissue of the cecum. Never were there found more than two bacilli in a single field and this was noted but twice —once in the glands and once in the cecal wall. Since those found were of very typical form and appearance it is safe to conclude that the comparatively negative results of the search were due to scarcity of the organisms.

From the absence of symptoms and physical findings pointing to localized tuberculosis in other parts of the body it would seem that this case is one of primary localized tuberculosis of the bowel. As is well known to medical clinicians, however, it is quite possible to have a slight apical involvement of the lung which may at certain times present no findings even upon the most careful physical examination. Especially is this true of small healed tuberculous foci in whatever part of the lung. From the comparative infrequency of primary tuberculosis of the bowel, which will be shown by statistics cited later, it is perhaps unsafe to conclude that this case is such a one though the clinical findings speak strongly in favor of it.

The second case of hyperplastic cecum tuberculosis which has come under my observation is an unoperated

one in which the disease was combined with carcinoma of the same organ. But one similar case has been noted in the literature at my disposal; that one is recorded by Salzer[23] in the surgical reports of diseases of the cecum from Billroth's clinic.

CASE 2. *Tuberculosis and carcinoma of cecum; inguinal fistula; death.*—Mrs. D., 54 years of age, entered the Presbyterian Hospital July 24, 1897, and was assigned to the service of Dr. N. Senn. On account of a misplacement of the hospital record only the following very brief abstract of the clinical history can be given. For this and the post-mortem report I take pleasure in expressing my thanks to Dr. J. D. Freeman.

There was no history of tuberculosis or malignant tumors in any member of the family. Three years before entrance to the hospital tumors were removed from the left breast and left axilla but there is no definite knowledge of their nature. The patient gave a history of a fall, receiving a blow in the right inguinal region. Succeeding this there was pain upon walking which radiated down the leg. Later there appeared a swelling in the right groin which was incised revealing an abscess. There remained to the time of death a fistula in the right groin which at times had permitted the escape of fecal matter. Repeated examinations of the pus from the fistula failed to show any actinomycelial granules. The patient died July 30, 1898.

Post-mortem examination.—Anatomical diagnosis: Right inguinal fistula communicating with the cecum; chronic tuberculosis of lungs and peri-bronchial lymph glands; amyloid spleen; chronic interstitial nephritis; carcinoma of the cecum associated with tuberculosis.

The body is that of an emaciated, old woman; rigor mortis slight. In the right inguinal region above the middle of Poupart's ligament are two sloughing fistulous openings from which escape upon slight pressure a thick, greenish-yellow purulent material.

The peritoneal cavity is empty and the peritoneum is smooth. The head of the cecum is bound firmly in the right iliac fossa by strong fibrous adhesions. The appendix is not recognized.

The pleural and pericardial cavities show no changes.

The heart is contracted. There is a "soldier spot" on the anterior surface of the apex. The pulmonary and aortic valves are competent to water. The cavities of the heart contain clotted blood. The endocardium is smooth and the valves show no changes. The myocardium is soft, of yellow-red color and has a greasy feel. The coronary arteries and the aorta show no changes.

The lungs are bluish in color and show a marginal emphysema. They crepitate throughout and float. In the center of

the middle lobe of the right lung is a firm pea-sized nodule with a calcareous center. The apices are free from changes. The peribronchial lymph glands are black upon the cut surface and have calcareous nodules in them.

The spleen is larger than normal and of firm consistence. The capsule is smooth and tense. It cuts with increased resistance. The pulp is firm and pale red. Everywhere on the surface are pin-point sized, translucent, slightly elevated, grayish areas.

There are two small cysts on the convexity of the left kidney. The capsule strips reluctantly, bringing away parts of the parenchyma and leaving a rough granular surface. Many small, irregular, yellowish, depressed scars are seen on the surface. On section the cut surface is pale. The cortex is to the medulla as 1 to 2½. The cortical markings are invisible. The pelvis of the right kidney is dilated.

The liver is smooth externally. The substance is soft. Cut surface is yellowish and feels greasy. The lobular markings are invisible. The gall-bladder is negative.

The stomach and small intestines are negative.

A soft catheter passed down through the right inguinal fistula appears in the cecum. Between the external opening and the opening into the cecum lies a cavity half the size of the fist and half filled by a fleshy looking mass. The cecum forms part of the wall of this cavity and projecting into the lumen of the head of the cecum is a large cauliflower-like mass. The anterior cecal wall is thick, firm and apparently fibrous. The remainder of the large intestine shows no changes.

The pelvic organs and pancreas show no changes.

Macroscopic examination of the cecum after hardening for several weeks in Müller's fluid and alcohol.

The mass is about the size of the fist or slightly larger. The anterior surface of the cecum presents a defect in the wall about 3 cm. in diameter, this defect being largely closed in by a soft, projecting tumor mass having a finely papilliform surface. The cecal wall adjoining this defect is 1 to 2 cm. in thickness and is firm and indurated. That side of the border of the defect lying toward the ileum is free from the papillary outgrowth and has a roughened internal surface. Section shows this thickening to extend along the anterior cecal wall for a distance of about 5 cm. to where it joins the small intestine and to extend backward over the caput coli to the posterior wall, which is not more than the usual thickness. Upon multiple sections of this wall on the side of the opening toward the small intestine it is seen to be composed largely of firm fibrous or fibro-muscular tissue and to contain one very large blood-vessel with a greatly thickened wall. There is also noted a somewhat crescent-shaped area in the center of each

section which is made up of a clear translucent substance presenting a glistening surface.

Upon cutting open the cecum longitudinally it is found to be practically filled by a cauliflower mass springing from the margins of the above noted defect in anterior wall and from the inner surface of the thickened wall lying posterior to that defect. The peripheral terminations of this papillary growth are fine and filamentous. Upon it are found a few firm, smooth, oval polypi the size of large wheat grains, and resting upon fine filamentous pedicles up to 1 cm. in length. The inner surface of the indurated and thickened portion of the anterior wall lying toward the ileum presents none of the papillary outgrowth and is apparently devoid of mucous membrane. It presents the appearance of shallow ulceration. The remaining mucosa and the wall of the cecum and of the adjoining bowel segments are free from visible changes. In two places the growth penetrates the posterior cecal wall and appears externally with the same general characteristics. Section through one of the large papillary masses shows a branching tree-like arrangement of connective tissues covered by what resembles a thickened mucous membrane. No connective tissue is visible in the finer terminal filaments. The remainder of the tissue is firm and fibrous with smaller and larger areas of yellowish fat. In sections of the wall posterior to the defect are noted a similar increase in firm connective tissue enclosing, however, larger and smaller masses of translucent gelatinous material.

Microscopic examination.—Sections through the tumor mass show it to be made up of a rich celled branching connective tissue framework bearing a thick layer of tubular epithelial structures. The tubes run in various directions and are in places coiled and bent upon themselves. The line of junction of the epithelial and connective tissue portions of the mass is sharply defined and the tubules do not penetrate into the deeper framework of the tumor. It has the appearance of a benign papillomatous proliferation of the mucous membrane. The epithelial cells are large and cylindrical, contain large oval nuclei near their basal attachments and show but a single layer to each tubule. Many of the glands are cystic. They show all stages of mucoid degeneration and some superficial necrosis with disappearance of the nuclei. In some places the mucoid material only fills the lumen of the tubule, the cells being free from it. This change is more noticeable in the deeper parts of the epithelial structure.

Sections of the thickened wall behind the defect in the cecum show toward the inner surface, at the base of the cauliflower-like mass, this same epithelial proliferation with extensive mucoid changes. The epithelial cells are here seen to penetrate to all depths of the tissue as discrete tubules, small masses of tubules or as tubules without visible openings, forming

strands of atypical epithelial cells. This formation even penetrates the entire thickness of the wall and shows masses of atypical tubules externally. In most of this formation the mucoid change is far advanced, resulting in partial or complete destruction of the protoplasm of the cells. There are found also large irregular areas of stringy, mucoid material into which project connective tissue strands, radiating from which is often a very definite penniform marking made by strands of mucoid of different densities. Following the line of this marking are occasionally seen rows of epithelial cells in an advanced stage of degeneration. These areas correspond to the gelatinous masses noted in the gross specimen. There is found also great hyperplasia of the fibrous elements of the wall and large areas of adipose tissue. In the stroma are a few small nodules of lymphadenoid tissue. Throughout the wall are scattered small areas of round-celled infiltration and at the border of the defect in the wall a superficial necrosis and diffuse round-celled infiltration.

Sections taken from the wall on that side of the defect toward the ileum, where in the macroscopic examination none of the tumor growth was found, present in some respects a strikingly different picture. There is the same connective tissue hyperplasia, which is here even more marked, there are small areas of mucoid material and areas of fat. The inner surface is made up of granulation tissue with superficial necrosis. Embedded in this granulation tissue are a large number of giant cells some of which have a definite peripheral arrangement of the nuclei and are surrounded by cells of ovoid and elongated shapes staining distinctly paler than the surrounding denser round-celled granulation tissue. Deeper in the tissue are small round-celled areas but no giant cells are found among them. In certain parts of the wall are found different sized groups of large oval or polygonal cells formed into a distinct alveolar arrangement by a delicate connective tissue stroma, the alveolar spaces containing one to ten cells each. From their size, shape, arrangement and staining properties these would seem to be atypical epithelial cells, but they do not otherwise resemble the carcinoma cell nests found in other parts and show no mucoid changes.

There is a considerable thickening of the walls of all the blood-vessels. In a mass of lymphadenoid tissue lying at the side of a large vessel there are noticed clear hyalin looking areas and wide hyalin zones lying just outside the endothelial lining of the small blood-vessels. These areas and zones stain purple with iodin green and are interpreted as amyloid.

In the enlarged retrocecal lymph glands are found several typical tubercles with central giant cells and a zone of pale epithelial cells surrounded by densely packed small round cells. There is no necrosis except in the central part of the giant

cells and no resemblance of caseation is noted. Amyloid material is present here also as small areas and zones in the capillary vessel walls. In the tubercles of these glands are found a very few tubercle bacilli. The search for tubercle bacilli in the base of the ulcer of the cecum and in the lymphoid areas of the cecal wall was negative.

We have not here the classical picture of hyperplastic cecum tuberculosis set forth in the first case, yet it seems plain from the great overgrowth of connective and muscular tissue in the wall—measuring 2 cm. in thickness—that the case belongs to the same class. From the few facts in the clinical history it seems more probable that this case is one of perforating tuberculosis of the cecum secondarily invaded by carcinoma. The fact that the inguinal fistula was of long standing speaks strongly for such a sequence. Further evidence is found in the macroscopic findings in that the malignant growth takes its origin from the margin of an old tuberculous ulcer. Though tubercle bacilli were not found in the base of this ulcer itself, it seems clear from the histological findings in the wall of the cecum and the presence of tubercles and tubercle bacilli in the adjacent lymphatic glands that the lesion must be of such an origin. There is a well marked extension of the tuberculous process to the regional lymphatic glands while the malignant growth remains localized in the cecal wall. In the lungs and peribronchial lymphatic glands there are found healed tuberculous foci which may have given rise to the development of the primary disease of the cecum.

II. PATHOLOGICAL ANATOMY.

As used in reference to the condition here considered the word tumor has only a clinical significance. However great the swelling may be it is essentially a hyperplasia; whatever may be its macroscopic resemblance to carcinoma or other true tumors it is distinctly an inflammatory swelling which Benoit[24] has termed "pseudo-neoplasm."

This hyperplastic form of tuberculosis as found in the intestines is usually located in the cecum and most often takes its origin at the ileo-cecal junction. A case was operated upon by Esmarch[25] in which there was in addition a similar tuberculous tumor in the ileum producing stenosis 35 cm. above the ileo-cecal valve. Sachs[4] calls attention to a similar tumor of the ileum in the practice of Kocher.

In the beginning the tumors are small and sharply outlined from the adjoining portions of the bowel. They are usually rough and nodular and may reach the size of a large orange. In the case reported by Sachs[4] the mass was 10 to 12 cm. in diameter. They lie above the brim of the true pelvis in the right iliac region and may be slightly movable or firmly fixed. Fibrous adhesions are usually found binding the cecal tumor posteriorly and it may be adherent to loops of intestine, the abdominal wall and other surrounding structures. Koerte[26] was compelled to abandon a radical operation on account of the bad local condition. The wall of the cecum is firm and unyielding, resistant to the knife, whitish on the cut surface, and is irregularly contracted by cicatrices. It measures in thickness from .5 to 3 cm. and often contains areas of firm fatty tissue. This thickening is as a rule confined to the cecum and its immediate neighborhood, the mass measuring little more in a direction parallel to the bowel than in its transverse diameter. In the case of Pilliet and Thierry[5] the change in the intestinal wall extended even as far as the sigmoid flexure. While such a condition is to be looked upon as a decided exception it is to be noted that the lesions have little tendency to extend to the ileum but more to continue up the large bowel, the wall being frequently thick and hard for a distance of several inches. The thickening is due to a hyperplasia of the fibrous and muscular tissues; the inelastic firmness to infiltration with tuberculous granulation tissue.

With but a single exception[12] in the recorded cases there has been more or less marked stricture at or near the position of the ileo-cecal valve. The stricture may be annular, canalicular or funnel shaped and is usually sufficiently marked that chronic intestinal obstruction is one of the clinical features of the case. The degree of constriction is sometimes excessive. In a case reported by Becker[27] water found its way through the narrowed lumen only in drops. In one of Czerny's[28] cases the narrowed lumen was divided into two equal parts by a fibrocellular band, left in the ulcerative process at the ileo-cecal valve. The narrowing may be caused by cicatricial contraction in the healing of old tuberculous ulcers but also by hyperplasia of the intestinal tunics and the formation of numerous polypoid outgrowths of the mucosa. The point of greatest constriction is usually at the ileo-cecal valve, which is thickened, stiff, cicatricial or often unrecognizable. Associated with the stricture at the location of the tumor it is not infrequent to find cicatricial stenosis in other parts of the bowel. Frank[29] found such a condition in both the ileum and the ascending colon. Czerny[28] found at a distance of two meters above the valve a constriction from a healed tuberculous ulcer, associated with tubercles on the peritoneum. Conrath[1] found stricture outside the cecum in 7 out of 81 cases. From the resistance to the progress of intestinal contents caused by the stricture there occurs a compensatory hypertrophy of the lower ileum, often associated with considerable dilatation of the lumen and induration of the wall. That the hyperplasia in the wall of the cecum itself is not brought about by constriction—that it is not a compensatory hypertrophy—is shown by the case of Caussade and Charrier[12] in which the cecum was dilated and there was no stricture at any point. The cecal wall showed great hyperplasia, as do cases with stricture, which was eccentrically developed.

Early in the disease the mucosa may be little changed. It is usually the seat of larger or smaller ulcers, with undermined edges and a floor beset with minute greyish tubercles. These may involve a large part of the colon and lower ileum as in cases of Pilliet and Thierry[5] and Czerny[28]. They may be serpiginous, even leaving islands of intact mucous membrane as in ordinary destructive tuberculous affections. In certain instances, however, a mucosa appearing entirely intact to the naked eye has been found in a relatively far advanced case of chronic cecum tuberculosis. Such are the cases reported by Sachs[4], Hofmokl[30], Goschl[31], and Case 1, reported in this paper. The mucosa is much thickened and beset with little papillomatous masses of variable size which constitute one of the striking and almost constant features of the gross pathology of the condition. They are largest and most numerous at the margins of the ulcers where they may reach the size of hazelnuts[5]. On the other hand they may be fine and filiform. As in Case 2 reported here they may be set upon long slim pedicles or by some accident of development buried in the wall, conditions which I have not found described in the literature. The papillæ are present also and in typical form in those cases not showing ulceration. Caussade and Charrier[12] describe a case in which the hypertrophied mucosa was simply thrown into numerous transverse folds which were in places branched or broken into segments. In a case from Czerny's[32] clinic a 2 cm. broad ring of cauliflower mass, which was ulcerated, soft and hemorrhagic, grew into the lumen. Following this was a 5 cm. broad cicatrix and following the cicatrix 9 cm. of ulcerated surface.

The vermiform appendix is usually found not greatly involved. In general it resists well though usually embedded in adhesions. The lumen usually opens freely into the cecum. Hartmann[33] reports a case in which it was greatly dilated and the lumen occluded. The sub-

mucosa is usually to some extent hyperplastic. In a case by Thierry and Routier[34] the appendix had undergone changes similar to those of the cecum.

Tuberculous changes in the retrocecal lymphatic glands are practically constant. The invasion is, however, limited to a few glands and they are not greatly enlarged. They are firm in consistency and show the same lack of tendency to gross degenerative changes noted in the cecum itself, though they are not infrequently found to have undergone caseation. In exceptional instances the lymphatic involvement is comparatively great and may extend even to the retroperitoneal glands lying along the aorta, which are transformed into a caseous mass. In a case by Auscher[35] this extended even to the subclavicular group.

The microscopic picture varies much, according to the original location, the rapidity of development and the amount of necrosis or healing in the affected areas. It has a special anatomical character in the hyperplasia of the fibrous and muscular elements of the wall, the villous bud-like outgrowths of the mucosa and the changes in the submucous layer. Its essential feature is, however, the tubercle. These are often grouped into small masses of sufficient size to be recognized by the naked eye. They may be confluent or discrete and show little tendency to become necrotic and disintegrate, as is usually the case with tuberculous tissue, but remain a long time in a state of anatomical preservation. With a decided tendency toward fibrous evolution they add not only to the thickness of the bowel wall but contribute to the stiffness and rigidity so characteristic of tuberculous tumors of the cecum. Many times the typical histological tubercle, with its giant cell and epithelioid cells, is substituted by a diffuse infiltration with small round cells, which led Pilliet[50] to call attention to the striking resemblance it often bears to sarcoma and to express the opinion that many cases had

been presented as malignant tumors. For similar reasons the condition is called "lymphoid tuberculosis" of the cecum by Courtillier[10]. Tubercles are usually most numerous in the submucosa which is entirely altered in structure by the presence of vast numbers of embryonal cells. There is a hyperplasia of the mucosa with the formation of tubercles and an enormous embryonal infiltration which may destroy the glandular elements almost entirely.

The polypoid outgrowths of the mucosa are usually covered by intact epithelial tissue and much infiltrated with round cells. Tubercles may be found in them or in the submucosa at their base. The pediculated forms which I have noted contained neither epithelial tissue nor tubercles and were made up of a rather richly cellular connective tissue with blood-vessels and a dense connective tissue capsule. The buried polypi all contained necrotic centers and an epithelium largely replaced by tuberculous granulation tissue.

There is a variable, but always well marked, thickening of the muscular coat of the bowel due to hyperplasia of muscular and connective tissue elements. Here also are found embryonal cells in limited areas, but tubercles are few or wanting. As a single exception to the general rule is a case reported by Rutier[36] in which the thickening of the wall was due to a caseous infiltration of the muscularis. There is also a hyperplasia of the subserous coat which usually contains a few tubercles and areas of adipose tissue. In a limited number of cases it has been noted that there is a distinct subserous type of the disease, the submucosa, constituting as it does the usual location, being here comparatively uninvolved. Such a case is recorded by Conrath[1] in which there was a diffuse subserous infiltration not histologically recognizable as tuberculous. In one of the cases of Hartman and Pilliet[3] the serous coat was three times as thick as the mucosa and one and one-half the thickness of the

muscular coat. There was also much round celled infiltration without tubercles in the subserous coat in the case of Pilliet and Thierry[5].

In much of the literature on the subject of tuberculosis of the cecum the tubercle bacillus is not mentioned. In a few cases it seems to have been easily demonstrated and abundant. In many, however, it is stated that the bacilli were exceedingly scarce and demonstrated with difficulty. It is safe to say that the tissues are usually very poor in bacilli. The retrocecal lymphatic glands are the seat of tuberculous disease of much the same general characters as that found in the cecum, showing the same scarcity of tubercle bacilli and lack of tendency to destructive changes, the condition being as a rule rather that of fibrous metamorphosis.

III. ETIOLOGY, PATHOGENESIS AND COURSE.

The statement of Benoit[24] that chronic tuberculosis of the cecum, as is the case in ordinary typhlitis, is found more frequently in males than in females, is not warranted by an analysis of the recorded cases. In 77 cases in which the sex was given Conrath[1] found that 36 were males while 41 were females. Adding to these the cases of Page[16], Lediard[17], Oschner[14], Senn[15], Caussade and Charrier[12], and those reported in this paper, we get 40 males and 44 females. Thus it seems that there is practically no difference in the susceptibility of the two sexes.

The majority of patients affected are between the ages of 20 and 40 years. Adding to the 75 cases collected by Conrath in which the age was given those mentioned above, it gives the following table of frequency for each decennium:

Age.	Male.	Female.	Total.
1 to 10	0	0	0
11 to 20	4	7	11
21 to 30	10	14	24
31 to 40	19	10	29
41 to 50	3	6	9
51 to 60	3	5	8

Occupation seems to have an influence only in so far as the abdomen is subjected to more or less violent and repeated pressure or trauma, thus producing a locus minoris resistentiæ. Suchier[37] relates a case in which a specific traumatic influence seems to bear directly upon the etiology. It is that of an agate-grinder in whom the abdomen was subjected to more or less constant pressure twelve hours daily. Case 2 of this paper also gives evidence of a traumatic influence. A number of cases have been noted in persons following pursuits in which the abdomen is liable to pressure, such as saddlers and shoemakers.

From certain cases following attacks of typhoid, dysentery and enteritis it would seem that acute infections or inflammatory conditions of the cecum play a part in the etiology. This agrees with the general etiology of tuberculosis in other parts of the body, the preceding inflammation lowering the resisting power of the tissues and furnishing a more favorable soil for the lodgment and development of the specific organism. Hansemann[38] has lately brought forward the subject of secondary infection of inflamed tissues with tubercle bacilli and cites a number of cases illustrating the process. One of these is that of a phthisical patient with typhoid fever in which there were found recent tubercles on the base of a typical typhoid ulcer. Similar cases are cited by Ernst[39] and Birch-Hirschfield[40]. The irritating effects of prolonged constipation and of foreign bodies exert a like influence.

The etiological influences noted above can not, of course, be more than predisposing to the localization and growth of the infectious agent in the cecum. This may reach the cecum by being taken with the food, especially milk and meat. From the known frequency of tuberculosis in cattle it would seem a reasonable inference that primary tuberculosis of the bowel should be a not infrequent condition. Basing conclusions upon the

statistics of various investigators it is safe to say, however, that intestinal tuberculosis is, in the vast majority of cases a secondary affection. This is almost universally true except in young children. In examining 1000 tuberculous subjects Eisenhardt[41] found tuberculosis of the intestine present 567 times. Of these 567 cases 563 were secondary to tuberculosis of the lungs and 3 were secondary to tuberculosis in other parts of the body. In the one remaining case the disease was found in the intestine only, but it was considered doubtful if it was a primary affection of that region. Frerichs[42] found but one case primary among 208 of intestinal tuberculosis and considered that one doubtful. Fenwick and Dodwell[43] found tuberculous ulcers of the intestine 500 times in 883 cases in which the lungs were the primary seat of the disease. Herxheimer[44] furnishes the very interesting fact that of 58 cases of phthisis sectioned from April to November, 1895, he found only one free from tuberculous lesions in the intestine. He quotes Weigert as saying that 90 per cent. of the phthisical patients in Leipsic have intestinal tuberculosis. These figures point toward two things: that intestinal tuberculosis is a very frequent secondary affection in phthisical patients, and that the vast majority of cases of intestinal tuberculosis are the result of swallowed tuberculous sputum. The simple enteritis which so frequently accompanies tuberculosis no doubt contributes largely to the frequent intestinal involvement, though as has been shown by Orth[45] and by Dobroklonsky[46] that tuberculous infection of the intestine may take place where there has been no preceding inflammatory condition even when the epithelial covering remains intact.

In the primary localization of tuberculosis in the intestinal tract it has been shown by Fenwick and Dodwell[43] that the cecum is far the most frequent site, the process usually spreading from here to the adjoining segments. They found the cecum involved in 85 per

cent. of all cases while that region alone was involved in 9.6 per cent. Frerichs[47] found the cecum involved in 80 per cent. The researches of Eisenhardt[41],, Spillman[48] and Girode[49], and others, show similar results. The frequency with which the disease is found present decreases in both directions from this point. The large dilation of the cecum and its independent position make it a favorable location for stasis; and by decomposition of the intestinal contents predispose to inflammatory processes, thus allowing for the easy implantation of tubercle bacilli. As has been shown by Ribbert[50] the cecum and appendix are also very rich in lymph follicles, and Tchistovitsch[51] has demonstrated that in the development of intestinal tuberculosis the lymphatic elements are first affected, the epithelial tissue being involved only secondarily by a spreading of the process from the follicles. The food or sputum impregnated with bacilli passes with comparative rapidity over the mucous membrane of the œsophagus and the small intestine. It finds a temporary resting place in the stomach, but here the adverse influence of the gastric juice, demonstrated by Wesner[52], prevents the development of the organism. The same influence is exerted to a less extent in the upper part of the small intestine.

But the real pathogenesis of chronic hyperplastic cecum tuberculosis is found in the answers to the questions: Why does one case remain localized when the greatest part, beginning as they do in the cecum, become quickly disseminated?—and—why does the same bacillus produce at one time gross ulceration and destruction and at another ulceration with hyperplasia? A review of the clinical histories and the post-mortem findings furnish a basis for explanation in that with active, destructive and disseminated tuberculosis of the intestine there is usually found in the lungs a similarly active process, while in cases of localized chronic cecum tuberculosis there is quite as frequently found a latent, healed

or healing pulmonary involvement. In the phthisical subject there is a lack of general resistance due to toxemia; the accompanying enteritis gives ample occasion and the constantly swallowed bacilli constantly add to the number of intestinal lesions as the disease advances in the lungs. The facility of extension may also be increased, as suggested by Benoit[24], by reason of abnormal ferments which enfeeble and irritate the mucosa. On the other hand in those cases where the lung tuberculosis is slow or healing, the general resistance to the tuberculous infection is good, there is not the same liability to accompanying enteritis, and a small number or no bacilli enter the gastro-intestinal tract. Thus the lesion is able to take a natural course in the conflict between tissue and organism and to pursue that most favorable to the tissue.

The nature of the process is essentially a slow, chronic inflammation of slight intensity. Practically all tuberculous cecal tumors are poor in bacilli, which may account for the chronicity of the process, though, as Tchistovitsch[51] has shown, caseous transformation does not depend upon the number of bacilli but rather upon their virulence. Infection with an attenuated race of organisms or an unusual resistance on the part of the tissue may also lessen the intensity of the process and give the tissue opportunity to protect itself. Hartman[3] suggests that the tuberculous ulceration may open an infection atrium to other organisms which contribute to the development of an attenuated tuberculosis. That simple tryphitis is transformed into tuberculous typhlitis is, however, the logical conclusion, and it has been lately shown by Ramond and Ravault[53] that tuberculous dissemination and destruction proceed more rapidly in the presence of even non-pathogenic bacteria.

In primary tuberculosis of the cecum the general conditions would be much the same as in that contracted from a healing pulmonary lesion. The clinical history

seems often to point to such a primary infection, but even where the physical examination fails to show any involvement of the lung there is found post-mortem an old lesion. On account of this slight involvement, or the inability to clinically demonstrate any at all when the tumor is first noticed, many authors have concluded the pulmonary affection secondary. Opposed to this view are two facts: the extreme rarity of localized cecum tuberculosis with no lung findings and the extreme frequency of slight, ancient pulmonary involvement. Even where a patient with a tuberculous cecal tumor has died of a later pulmonary tuberculosis there has been found evidence of an old latent or healed preceding process which may have given rise to the cecal trouble.

As has been already noted there occurs a subserous form of cecum tuberculosis leading to hyperplasia and tumor formation. This has been explained by some writers as a hematogenous metastasis from the lungs. It has been shown, however, that hematogenous metastasis does not often occur in the intestines. Upon the basis of pathological anatomical findings Conrath[1] gives another explanation. 1. In children the mesenteric glands of the cecum are often found swollen, the enlargement being due to tuberculosis. According to the researches of Orth[45] and others the intestinal canal may admit tubercle bacilli to pass through without itself becoming the seat of disease. Of 9 rabbits in which tuberculosis was produced by feeding the bacilli only 7 showed lesions of the bowel; and the intestinal canal of young children is said to be easily permeated by them, the leucocytes playing a large part in the transmission. 2. In young individuals a peritoneal tuberculosis from tuberculous mesenteric lymph glands is not infrequent. Hence after simple typhlitis or trauma a tuberculosis, resting in the lymphatic glands since childhood—not an infrequent condition—may spring into activity and lead to localized tuberculous peritonitis of the cecal

region and to subserous cecum tuberculosis of slight intensity and chronic course. The lymphatic glands lie so close behind the cecum or in its mesentery that the infection can easily pass over. He refers to the case of Suchier[37], cited elsewhere, in which there was a specific traumatic agency. When both forms are present, he concludes, they are from independent sources of infection, the submucous causing the development of the subserous from a resting tuberculous gland.

If tuberculosis is limited to the cecum and not associated with an active pulmonary involvement its progress is slow and sooner or later a tumor appears which reaches a variable size. With failing nutrition and general health, due to chronic obstruction, the tissue is ultimately unable to resist the infection and to go on with its excessive repair, and necrosis and abscess formation is a very probable consequence. By the agency of preceding adhesions, which are firm and fibrous, when such a result comes the abscess breaks into a securely walled off cavity and appears as a localized suppurative peritonitis. The abscess may, however, either primarily or secondarily break through the abdominal wall. This condition then presents three possibilities: fecal fistula, anus præternaturalis or spontaneous healing. The latter is not, however, a frequent result; and old sinuses, discharging either the pus or a mixed infection of fecal matter, are likely to persist throughout the patient's life.

Extension of the disease may be by the peritoneum itself, resulting in a tuberculous peritonitis, a comparatively rare result; it may be by the bowel itself and is then, as already noted, usually in the direction of the colon, resulting either in gross ulceration or in a continuation downward of the hyperplastic process. Its progress is in general by way of the mesenteric lymphatics, the retroperitoneal glands becoming involved, as the lesions advance. It rarely if ever travels by way of the blood stream.

TUBERCULOSIS AND CARCINOMA.

Theoretical considerations and clinical experience led Rokitansky[54] to believe that carcinoma and tuberculosis maintained a mutual immunity. In the later editions of his work he comes more and more to give up this theory and asserts only that the two diseases are not usually combined and that where they do co-exist it is the rule that the carcinoma follows the tuberculosis.

Rokitansky found early opposition to his theory by Lebert[55]; and against the theory stands a mass of statistics concerning the finding of both diseases present at post-mortem, Sandu-Miclesco[56] found among 150 cases of carcinoma 9 per cent. combined with tuberculosis. Rapok[57] found 39 tuberculous among 399 carcinomatous subjects. Loeb[58] found among 111 carcinomatous 31 cases combined with tuberculosis, while Cahen[59] found that among every 20 cases of carcinoma or 50 cases of tuberculosis there occurs one case in which the two are combined. Williams[60] goes so far as to say that the same conditions predispose to both diseases and that survivors in tuberculous families are much more liable to carcinoma in old age than are other persons. He found that 55 per cent. of 134 cases of carcinoma of the breast came of tuberculous families; and that while the ratio of deaths from tuberculosis in the community at large was 1 in 11, in the parents of the carcinoma patients it was 1 in 3.8.

The investigations of Lubarsch[61], while showing likewise the frequent combination of the two diseases leads him to a different conclusion concerning their relations. He found in a series of 6536 autopsies 569 cases of carcinoma, in 117, or 20.6 per cent. of which, tuberculosis was also present. In a complete review of the cases, however, he found that of the non-carcinomatous 3.7 per cent. more were tuberculous than of the carcinomatous; and of the non-tuberculous 1.05 per cent. more were carcinomatous than of those showing also tubercu-

lous lesions. His conclusion that there is a certain degree of antagonism between the two conditions, which he attemps to explain in that carcinoma may produce delicate chemical changes in the blood injurious to micro-organisms, is liable to error, as suggested by Naegeli[62], in two ways; many fall victims to tuberculosis before the age of forty, when we would not expect to find carcinoma, or, an old healed tuberculosis or a beginning carcinoma may be overlooked. But these statistics furnish the valuable fact that the two diseases are often associated in the same body.

Especially destructive to the theory of Rokitansky are those cases in which the two pathological processes are found simultaneously present and active in the same organ. Epithelioma taking its origin upon an old lupus of the skin was early recognized; but the first well authenticated case of combined tuberculosis and carcinoma involving a mucous membrane is reported by Zenker[63]. There was a squamous-celled epithelioma of the esophagus with a round ulcer, showing at the edges epithelial pearls and typical tubercles some of which were caseous. Tubercle bacilli were present in moderate numbers. In a second case reported at the same time, in which the larynx was involved, it was impossible to demonstrate bacilli though they were typical histological tubercles. A second case in which the disease was located in the larynx of a man 54 years of age is recorded by Crone[64]. It presented itself clinically as a carcinoma and the microscopic examination revealed also a tuberculous proliferation of the submucosa in which the bacilli were demonstrated. A similar case was observed by Baumgarten[65]. It occurred in a woman of 44 and metastases in the thyroid and lymphatics showed both carcinoma and tuberculosis in typical form. Bacilli were not to be demonstrated in this case. Cases of carcinoma developing in old tuberculous cavities of the lung are reported by Friedländer,[66] Wolf[76] and

Schwalbe.[68] Claude[69] found in the body of a man dead of pulmonary and intestinal tuberculosis a carcinomatous ulcer of the stomach, in the base of which were found giant cells and tubercle bacilli.

When the oppositional theory was proven false the question naturally arose: do the two diseases stand in any causal relation and if so which is primary?

Concerning the manner of combination Lubarsch[61] distinguishes five possibilities: 1. Purely accidental association. To an old healed tuberculosis there is added a carcinoma without in any way influencing or being influenced by the tuberculous affection. To this class belong half of all cases. 2. By the side of an old tuberculous affection with fresh miliary tuberculosis, especially when generalized in the serous membranes, there is found a spreading metastatic carcinoma. In such a case the combination is attributed to the cancer cachexia making a more favorable soil for the tubercle bacillus so that a new tuberculous infection takes place from the old colonies. Such cases are not frequent. 3. To a well developed carcinoma there may be added a new tuberculous infection. Such cases are infrequent; Lubarsch could find but three cases in his extensive material; the cases of Zenker[63] and Claude[69] are to be considered as belonging to this class. Lubarsch considered it in no way proven that tubercle bacilli could more easily infect carcinomatous subjects. 4. There may develop a carcinoma upon a chronic progressive tuberculosis. The conclusion is here warranted that there exists an etiological relation between the two, the tuberculosis acting not a s a direct but as a predisposing cause as trauma or chronic irritations act as predisposing causes for the development of malignant tumors. 5. Simultaneous development of the two diseases—theoretically possible but difficult of demonstration.

It is very difficult to explain how a carcinoma of

the stomach stands in any causal relation with an old healed tuberculous focus in the lung. It is different when the two are located in the same organ. That the resulting cachexia and altered physiological functions of the one gives rise to the development of the other has had many upholders; and that this may influence some there can be no doubt, but Naegeli[62] noticed that in many carcinomatous bodies at Zurich there were also tuberculous foci which had not been made more active. In other cases he noticed that with the development of carcinoma a miliary tuberculosis set in and thinks that the carcinoma determined the development of it. That the tuberculous cachexia determines the development of the carcinoma does not find upholders in the literature. Certain cases point quite clearly to a secondary infection of malignant ulcers with tubercle bacilli, as the cases of Zenker and Claude. But this is not a frequent condition and careful consideration in the majority of reported cases of combination points to an old tuberculous focus-caseation, calcification, cavern formation, etc.

Ribbert[70] has insisted strongly upon carcinoma as the direct causative agent and reports eleven cases in different parts of the body (six of the lip, one each of the pharynx, tongue, eyelid, penis and mucous membrane of the mouth) in which he found giant cells between the advancing strands of carcinoma tissue. He was unable to demonstrate the bacillus and raises the question as to whether the growing tumor may not excite the formation of giant cells after the manner of foreign bodies. He does not dispute this possibility but gives it as his opinion that the tuberculosis preexisted. In accordance with his theory of the development of carcinoma being due primarily to an over proliferation of the subepithelial connective tissue,[71] he looks upon the tuberculosis as the direct causative agent of the malignant growths.

Clement[72] believed on the other hand that the cachexia dependent upon a developing carcinoma gives an excellent opportunity for a fresh tuberculous infection or the renewed development of an old focus and thus often determines an active tuberculosis. In reviewing the work of Ribbert he admits the tuberculous nature of but one of the eleven cases. He attributes the giant cells to the irritating action of the advancing carcinoma or to the presence of real foreign bodies, which Krückmann[73] has shown to be frequently present in the granulation tissue so often accompanying malignant growths. In support of his theory of the causative action of carcinoma cachexia Clement cites four cases. In the first there was an acute development of tuberculous adenitis of the submaxillary glands upon the appearance of a carcinoma involving the mucous membrane of the mouth; the patient had been operated upon for tuberculous glands of the neck in early life. In the second case a tuberculous adenitis of the axilla followed a carcinoma of the breast of the same side; the adenitis was attributed to bacilli wandering under the influence of the mammary carcinoma from a resting focus in the lung. The third case is considered one of congenital implantation of tubercle bacilli in the liver which awaited the cachexia of a carcinoma of the stomach for their development. The fourth case concerns a perivascular endothelioma of the parotid developing in tissue already tuberculous and determining a greater activity of the primary disease.

Not many authors are willing to attribute the causative role to the tuberculosis and yet this is the most probable thing in the vast majority of cases. After reviewing the literature Naegeli[62] gives it as his opinion that in all reported cases careful examination points to the presence of an old tuberculous focus. This opinion is shared by Ribbert[70] and partially upheld by Lubarsch,[61] Crone,[64] Wolf[67] and others. The correct-

ness of Naegeli's conclusion seems to be borne out by an examination into the case reports. In the fourth of Clement's[72] cases, for instance, the tuberculosis is plainly the older process; and, even granting that the cachexia caused by the tumor caused an increased development of the infectious process, it is not at all impossible that the tuberculosis aided in causing the development of the cancer.

Carcinoma is a comparatively frequent consequence of lupus of the skin and it can here be easily seen which is the older process. The opposite may occur but it is certainly not frequent. A certain number of the so-called lupus-carcinomas develop in the scars of healing; but here the inflammatory process acts indirectly as a cause. It is easily seen how chronic tuberculosis might predispose to the development of carcinoma by acting as a chronic irritation or by leaving scars in which carcinoma is prone to develop.

I have no hesitation in concluding that in Case 2 the tuberculosis of the cecum was the primary affection and bore a direct etiological relation to the succeeding malignant transformation. The carcinoma seems to have taken its origin from the margin of an old tuberculous ulcer and to have begun as a benign papillomatous growth —the almost constant accompaniment of chronic cecum tuberculosis. Naegeli[62] draws a like conclusion concerning a somewhat similar case of combination of the two diseases in the ileum, lacking, however, the extreme connective tissue and muscular hyperplasia noted here.

I take this opportunity of thanking Prof. Hektoen for material and counsel in the preparation of this paper, Prof. Senn and Dr. Morehead for the use of cases and Mr. Martin H. Fischer for his excellent drawing.

REFERENCES.

1 Conrath: Ueber die lokale kromische Cæcumtuberculose und ihre chirurgische Behandlung. Beitrage zur klinischen Chirurgie, Bd. xxi, 1898.

2 Billroth: Wiener Medicinische Presse, 1891.

3 Hartman et Pilliet: Bull. Soc. Anat. de Paris, 1891.

4 Sachs: Ein Beitrag zur Extirpation des Blinddarms wegen Tuberculose. Archiv. fur klin. Chir., Bd. xlii, 1892.

5 Pilliet et Thierry: Contribution a l'etude de la tuberculose locale du cæcum. Le Progres Medicale, Tome 20, 1894.

6 Czerney: Beitrage zur klinischen Chirurgie, Bd. vi, 9 u. 17.

7 Salzer: Beitrage zur Pathologie und chirurgischen Therapie chronischen Cæcumerkrankungen. Archiv. fur klinische Chirurgie, Bd. xliii, 1892.

8 Hofmeister: Beitrage zur klinischen Chirurgie, Bd. xvii.

9 Konig: Die stricturende Tuberculose des Darms und ihre Behandlung. Deutsche Zeitschrift fur Chirurgie, Bd. xxxiv.

10 Courtillier: Tuberculose chronique de l'angle ileocæcale. Bull. de la Soc. Anat. de Paris, 1896, No. 13.

11 Benoit: Tuberculose locale cronique de la region ileocæcale. Thesis. Paris, 1893. Abstract in Ergebnisse der Allgemeinen Pathologie, Lubarsch-Ostertag, 1895, Bd. ii, S. 337; also, Tuberculose ileo-cæcale chronique. Gazette des Hopitaux, 1898, pp. 357, 385.

12. Caussade et Charrier: Un cas de tuberculose ileo-cæcale a form hypertrophique avec considerations clinique, anatomique et therapeutique. Arch. Generales de Medicine, N.S. Tome, i, No. 4, 1899.

13. Beck: Annals of Surgery, Vol. xx. p. 672, 1894. S. Magill. Resection of the Ileo-cæcal Coil of Intestine.

14. Ochsner: Report of cases of Resection of the Cecum. Chicago Medical Recorder, Vol. ix, p. 113, 1895.

15. Senn: The Surgical Treatment of Intestinal Tuberculosis. Jour. Am. Med. Assn., Vol. xxx, No. 21, 1898.

16. Page: The Lancet, 1897, Vol. ii, p. 10.

17. Lediard: The Lancet, 1898, p. 408.

18. Orth: Lehrbuch der specielen path. Anat., 1887.

19. Zeigler: A Text-Book on Special Pathological Anatomy, 1897. Translation of eighth German edition.

20. Birch-Hirschfield: Lehrbuch des specielen path. Anat.

21. Konig: Handbuch der specielle Chirurgie, Siebente Auflage, 1898, Bd. ii, S. 330

22. Moorehead: Intestinal Obstruction. Chicago Clinic, Jan., 1899. A brief clinical history of Case 1 was furnished with others in this paper.

23. Salzer: Beitrage zur Pathologie und Chirurgischen Therapie cronischer Cæcumerkrankungen. Fall 19. Arch. f. klin. Chir., Bd. xliii, S. 101, 1892

24. Benoit: Gaz. des Hopitaux, 1898.

25. Esmarch: Quoted by Hofmeister. Uber multiple Darmstenosen tuberculosen Ursprungs. Beitrage z. klin. Chir., Bd. xvii.

26. Koerte: Deutsche Zeitschrift fur Chirurgie, Bd. xl, S. 562.

27. Becker: Ueber Darmresectionen Deutsche Zeitschrift f. Chir., Bd. xxxix, 1894, Fall 31.

28. Schiller: Ueber die Darmoderationen an der Heidelberger chirurgischer Klinik. Beitrage z. klin. Chir., Bd. xvii, S. 603, Fall 9.

29. Frank: Wiener klin. Woch., 1892, S. 390.

30. Hofmokl: Weiner klin. Woch., 1890, S. 878,

31. Goschel: Aertzlicher Local verein Nurmberg. Munchner Med. Woch., 1895, S. 251.

32. Czerney und Birdfleisch: Operationen am Magen und Darm.

33. Hartman: Bull. de la Soc. Anat. de Paris, 1892, p. 157.

34. Thierry et Routier: Quoted by Caussade et Charrier. Loc. cit.

35. Auscher: Quoted by Caussade et Charrier. Loc. cit.

36. Rutier: Cited by Conrath. Loc. cit., p. 90.

37. Suchier: Beitrage zur operative Behandlung der Cæcumtumoren. Berliner klin. Woch., 1889, S. 617.

38. Hansemann: Die secundare Infection mit Tubercle-bacillen. Berliner klin. Woch., 1898, S. 233.
39. Ernst: Quoted by Hansemann. Loc. cit
40. Birch-Hirschfield: Ibid.
41. Eisenhardt: Ueber Haufigkeit und Vorkommen der Darm-tuberculose. Inaug. Diss., Muncher, 1891. Abstract in Baumgarten's Jahresbericht, 1891, S. 824.
42. Frerichs: Quoted by Conrath. Loc. cit.
43. Fenwick and Dodwell: Perforation of the Intestine in Phthisis. The Lancet, 1894, ii, p. 133.
44. Herxheimer: Ueber Tuberklebacillen in verschlossenen verkasten Darmfollikeln. Deutsche Woch., 1895, S. 891.
45. Orth: Lehrbuch der specielen path. Anat., 1887, Bd. i, S. 839.
46. Dobroklonsky: Quoted by Tchistovitsch. Loc. cit.
47. Frerichs: Beitrage zur Lehre von der Tuberculose, 1882. Quoted by Orth, Loc. cit., p. 841.
48. Spillman: 1878. Quoted by Fenwick and Dodwell. Loc. cit.
49. Girode: 1888. Ibid.
50. Ribbert: Virch. Arch., Bd. cxxxii, S. 66.
51. Tchistovitsch: Contribution a l'etude de la tuberculose chez l'homme. Annales de l'Institute Pasteur, Tome 3, p. 209.
52. Wesner: Kritische und experimentale Beitrage zur Lehre von der Futterurgstuberculose. Habilitationsschrift. Freiburg, 1885. Quoted by Conrath, Loc. cit.
53. Ramond et Ravault: Action des microbes sur le developpement du bacille de la tuberculose. Arch de Med. Experimentale, Tome xi, No. 4, p. 494, 1899.
54. Rokitansky: A Manual of Pathological Anatomy, Vol. i, p. 313. Trans. for the Sydenham Society. London, 1854.
55. Lebert: Beitrage zur Kentniss des Gallertkrebses. Virch. Arch., Bd. iv, S. 214.
56. Sandu-Miclesco: Quoted in Ergebuisse der Allgemeinen path. Morph. u. Phys., Lubarsch-Osterag, Jahr. i, Abt. 2, S. 466.
57. Rapok: Ibid.
58. Loeb: Ibid.
59. Cahen: Ibid.
60. Williams: Observations on the General Pathology of Cancer. Medical Chronicle, Vol. xvii, p. 232, 1893.
61. Lubarsch: Bemerkungen ueber das gleichseitige Vorkommen von Krebs und Tuberculose. Virch. Arch., Bd. cxi.
62. Naegeli: Die Combination von Carcinom und Tuberculose. Virch. Arch., Bd. cxlviii.
63. Zenker: Carcinom und Tuberculose im selben Orgon Deutsches Arch. f. klin Med., Bd. xlvii, S. 191, 1890.
64. Crone: Arb. a.d. Tubinger path. Inst., Bd, ii, Hft. 1. Abstract in Baumgarten's Jahresbericht, 1893, S. 756.
65. Baumgarten: Ibid.
66. Friedlander: Cancroid in einer Lungencavern. Fortschritte der Medicin, 1885, S. 307.
67. Wolf: Der primare Lungenkrebs. Fortschritte der Med., 1895, S. 725.
68. Schwalbe: Entwickelurg eines primaren Carcinoma in einer tuberculosen Cavern. Virch. Arch., Bd. cxlix, S. 329.
69. Claude: La Semaine Medicale, T. 19, No. 5.
70. Ribbert: Carcinom und Tuberculose. Munchner Med. Woch., Bd. xli, No. 17, 1894.
71. Ribbert: Beitrage zur Histogenese des Carcinoms. Virch. Arch., Bd. cxxxv, S. 433.
72. Clement: Ueber seltenere Artn der Combination von Krebs und Tuberculose. Virch. Arch., Bd. cxxxix, S. 35.
73. Kruckmann: Abstract in Ergebnisse der Allgem. Path. u. path. Anat., Lubarsch-Ostertag, Jahrgang. i, Abt. 2, S. 467.

HYPERTROPHIC CIRRHOSIS OF THE CHICKEN'S LIVER.

N. W. JONES.

These specimens are sections of an hypertrophic cirrhotic liver weighing 250 grms., i. e., five itmes the normal weight of a chicken's liver. The surface of this organ is of light yellow color and perfectly smooth. It is devoid of all granulations or nodules. It cuts with markedly increased resistance. It is very hard and on cut surface shows no lobular markings at all. Sections of the tissues show that the hyperplastic connective tissue has not limited itself to the interlobular areas, but has developed intralobularly to a large degree, thereby arranging the cords of liver cells in peculiar nest-like groupings, the cells of which present more or less acute degenerative changes. The connective tissue is largely granulomatous in nature. It completely obliterates the original lobulation of the organ and constitutes by far the greater portion of its bulk. The liver presents, withal, the result of a very acute productive inflammation.

April 10, 1899.

SARCOMA OF THE CHICKEN'S LIVER.

N. W. JONES.

Case 1.—This specimen shows a fairly typical case of multiple sarcoma of the liver, weighing 100 grms., that was removed from a well-nourished chicken. The surface is studded with yellowish white nodules, varying in size from a few mm. to perhaps 2 cm. in diameter. On cut surface it is seen that they extend deep into the liver substance, and are well-marked off from the surrounding hepatic tissue, which appears reddish

brown in color. From the cut surface of these nodules a greyish viscid fluid can be expressed. Microscopically they are seen to be small round celled sarcomatous growths. Lying between them the liver cells are found deranged and more or less atrophied.

Case 2.—A somewhat more interesting case is that of a second sarcomatous liver, weighing something over 300 grms., which was removed from a greatly emaciated fowl. Its surface is smooth and uniformly greyish-yellow in color. Its most striking characteristic is that the growth has taken place uniformly save for a slight elongation, so that the original form of the lobes has been well preserved. On cut surface it is also greyish-yellow throughout; is coarsely granular and of soft consistency. It is slightly oily to the feel, and no lobular markings can be seen.

Histological sections show a very uniform growth of small round cells that lie in irregular groupings throughout the liver substance. These groupings have followed the original lobulation of the organ, so that the stroma consists in part of the connective tissue trabeculæ of the capsule. Thus the form of the lobule has been partly retained, but its elemental structure entirely obliterated. The few hepatic cells remaining are found pushed far to the side, next to or incorporated within the proliferated stroma. These cells have undergone considerable pressure necrosis. The old interlobular blood-vessels and bile ducts are largely preserved. Multiple sections of the liver show that there existed no portion of the organ into which the tumor cells had not penetrated.

Case 3.—A second infiltrating small round celled sarcomatous liver weighing over 800 grms., was examined, but as its structure, both gross and minute, closely resembled the last one, it need not be further described.

April 10, 1899.

Dr. N. Eisendrath presented specimens of intussusception in a child, June 14, 1897.

T. R. Crowder presented specimens showing a spontaneous gastro-enterostomy from neoplastic ulceration March 13, 1899.

THE GENITO-URINARY SYSTEM.

TUBERCULOUS GLOMERULITIS.

THE EARLY CHANGES IN THE GLOMERULI IN A CASE OF DIFFUSE MILIARY TUBERCULOSIS.

MARX WHITE.

Much has been written about the early changes in the various organs and tissues of the body in tuberculosis, and experimental work has been done to determine, if possible, the earliest pathological process produced by the lodgment of tubercle bacilli. The result of this work has been to show that the process varies, and that, too, often without known causes, but dependent as a rule upon well recognized conditions, as resisting power and anatomical pecularities of the tissue, number and virulence of the bacilli, and the mode of invasion, whether by lymph channel or blood stream, and if by the latter, whether singly, in small groups, or in larger emboli.

The kidney, on account of its anatomical peculiarities, particularly the arrangement and caliber of its vascular mechanism, affords rich ground for study along this line. The value of this organ for studying the influence of vascular conditions is enhanced 1, by the "terminal" arrangement of its arteries, and 2, by its non-liability, under ordinary conditions, to bacillary invasion by way of the lymph channels. Particularly is this true of the glomerular loops, which probably are wholly vascular, the transuded fluids being caried away by the urinary channels, rather than being picked up again by neighboring lymphatics.

It is to illustrate one of the less frequently described early tissue changes, of which I can find only three or four examples in the literature, that I present these specimens.

Arnold[1] found glomeruli in the centers of some small, tubercular nodules, showing accumulation of lymphoid cells in the walls of the capillary loops. Bowman's capsule was surrounded on one or all sides, by a layer of lymphatic tissue, varying in thickness. He noted also, changes in the epithelium of Bowman's capsule; sometimes the cells were only swollen and cloudy, sometimes showing proliferation, and often accumulating in the capsule in a crescentic mass, in which karyokinetic figures were occasionally demonstrable.

Baumgarten[2], in an experimental study, found the first histological changes in the kidney tissue invaded by the bacilli, to be multiplication of the fixed tissue cells. These cells were of the epithelium of the urinary tubules, glomerular capsule, and of the endothelium of the intertubular capillaries and the walls of the glomerular loops.

Nasse[3] described a case in which there was an eruption of tubercles along the entire distribution of an arterial twig as a result of tuberculosis of the arterial wall. He found several glomeruli, in the region of which little or no cell-growth was seen, but in which there was considerable change in the capillary loops. Some of these were impervious anuclear, and contained a finely granular mass with numerous bacilli, while remaining loops were perhaps more rich in nuclei, but sometimes appeared little changed. He found also the desquamation of the epithelial cells of Bowman's capsule forming a sickle or crescent shaped mass, more or less filling the capsule, in which case there was always at least a slight pericapsular cellular infiltration.

Hauser[4], in describing the renal lesions in a case of miliary tuberculosis, says:

"In the earliest stage, in the glomeruli we see an accumulation of immense numbers of tubercle bacilli, in single loops of glomeruli. Affected loops appear swollen and as though filled with a finely granular mass, while the glomerular epithelium does not take the stain, i. e., is necrotic. No further changes are seen in the glomeruli—neither proliferation of glomerular epithelium, nor inflammatory cell infiltration. In the stage immediately following, . . . we see a considerable growth of the tissue. The bacilli are now in thick, matted heaps. . . . On the solid loops, filled with bacilli, the epithelium is entirely destroyed, while on the neighboring loops, usually containing a few bacilli, a multiplication of the epithelial cells is demonstrable."

Durand Fardel[5] speaks of the frequency with which glomeruli are found in the centers of tubercles, and sums up his findings by giving the following "Localizations of Bacilli:"

1. In vessels and glomeruli, without tubercular or irritative products.

2. In vessels and glomeruli included in tubercular granulation tissue.

3. In convoluted tubules.

The anatomical diagnosis in my case is as follows:

Case 5002.—Cook County Hospital. Man, aged 54; chronic pulmonary tuberculosis with cavities; chronic tuberculosis of the larynx, the intestines, the right adrenal, the peribronchial and mesenteric lymph glands; miliary tuberculosis of the lungs, the spleen, and the kidneys, large white kidneys.

This case illustrates well the form of lesion described by Hauser, and shows, I think, the earliest changes set up by the bacilli. That the latter reached the kidney through the blood stream, there can be little doubt, the spleen also showing numerous minute lesions, containing bacilli, but invisible to the unaided eye.

In the kidney, the earliest change seen is in one

glomerulus, in which a single loop is converted into a finely granular mass, with the center filled with bacilli, most of which are radially arranged. The capillary endothelium is completely necrosed, and the whole little round mass is clearly marked off from surrounding loops, all of which contain blood, apparently in more than the usual amount, though this congestion of the glomerular loops seems general throughout the specimens. There is no demonstrable cellular increase in or about the glomerulus.

Many of the glomeruli show small necrotic areas, occupying one-quarter to a third or more of the whole, invariably containing numerous bacilli, sometimes so closely packed in the area as to give a bright red color, when seen with low power in specimens stained with hæmatoxylin and carbol-fuchsin. In several of these glomeruli there is little or no evidence of irritation, while in others, there is demonstrable increase in the number of cells, and the lumina of some or all of the capillary loops may be thereby obliterated. The new cells found in the glomeruli are apparently formed from the fixed tissue cells—they are distinctly endothelial in type, and an occasional epithelial cell is seen. Polymorphonuclear cells are few.

In none of the glomeruli showing the type of lesion above described can I find any considerable increase in the epithelium lining Bowman's capsule, so that the crescentic masses described by Arnold, Nasse and Baumgarten, are wanting. On the contrary, if the necrotic area is of any considerable size, and lies next the capsule, the epithelium here is, as a rule, necrotic, and the necrosis may extend a short distance into the surrounding tissue, and in such cases the bacilli are found to have passed beyond the glomerulus, and into the surrounding tissue.

The cellular infiltration about the glomeruli apparently begins when the bacilli have reached the periglo-

merular tissue from the necrotic mass as a starting point, for in none of the lesions young enough to be intelligible was the periglomerular infiltration present without the necrosis in the glomerulus, and the bacilli were apparently more numerous in the necrotic mass which was invariably adherent to the capsule and from which as a center, the bacilli appeared to be spreading. The area infiltrated varied from barely perceptible to an area as wide as the glomerulus itself, which it usually surrounded part way, forming a semilunar area outside of, instead of in, the capsule, with the necrotic glomerular loops lying next to the concave side.

In these areas, lymphoid cells predominated—small, with round, deeply staining nuclei; some epithelial cells were present, and here and there the tubular epithelium would take part, though for the most part, this was too much degenerated, as a result of the diffuse nephritis, to divide. No giant cells were seen.

Besides these early lesions there were numerous, typical, minute miliary tubercles, especially thick beneath the renal capsule, with necrotic centers and showing typical giant cells. An appearance seen in a few of these was the following:

In the center a round mass, the size of a glomerulus, but completely necrosed, and laden with bacilli. In two cases, this was surrounded by a row of somewhat swollen, but still brightly staining cells, and still outside this, the typical tuberculous tissue, as yet showing no caseation. Many of the tubercles contained numerous glomeruli, but as a rule these were shrunken, or nearly obscured by the dense cellular infiltration.

Throughout the cortex were many glomeruli with crescentic masses of desquamated epithelial cells in the capsule, but the presence of the diffuse nephritis above referred to, makes the cause of this condition uncertain, owing to its frequency in nephritis. In none of these were any necrotic areas found, nor could tubercle bacilli

be seen, either in the cell masses, or in the glomeruli. One thing attracting attention, however, was the frequency with which these glomeruli were found in the neighborhood of tubercles, with the crescentic mass on the side toward the tubercle as though the latter was the source of irritation.

The chemical nature of the necrotic masses in the glomeruli is hard to determine. It does not stain like hyaline. Weigert's fibrin stain gave negative results. With carbol-fuchsin and methylene blue it stains faintly red, and with hæmatoxylin, faintly blue; in fact, it reacts like simple necrotic or caseous material. Methylene blue and Gram's anilin, gentian violet stain fail to show organisms other than the tubercle bacilli.

The process is apparently a simple necrosis. That it is due to mechanical conditions alone, i.e., plugging of the vessel by small emboli, seems improbable, as the area is so small it might easily be nourished by the surrounding capillaries.

Does it not seem more probable that there is the added element of overwhelming toxæmia, the poisons brought there in large amounts of the bacilli or rapidly elaborated after the deposition and with the development of new bacilli?

If we discard the purely mechanical view, we must consider some such hypothesis to account for the necrosis, without precedent tissue proliferation and infiltration, processes which are supposed to occur, as a rule, before the necrosis, in tuberculosis.

The process described would resemble to a certain extent, in the early stages, the focal necroses found in the various organs in acute infectious diseases, as pneumonia, diphtheria, typhoid fever, etc., and LeCount[6] has described such local necroses occurring in the liver and spleen, in cases of tuberculosis.

No positive conclusions can be drawn from such an isolated case, and experimental work is needed to throw

light upon some of the questions involved, particularly as to the importance of the mechanical factor in these circumscribed necroses in the glomeruli.

1. Virchow's Archiv , 1865, lxxxiii.
2. Zeitch. f. kl. Medicin., 1885, x.
3. Virch. Arch., 1886, cv.
4. Deutsch. Arch. f. kl. Med., 1887, xl.
5. Arch. de Phys. 1886, vii.
6. Journal of Experimental Medicine, 1897, 2.

HYPERNEPHROMA.

CLINICAL REPORT OF A CASE AND DESCRIPTION OF THE TUMOR REMOVED BY NEPHRECTOMY.

L. L. M'ARTHUR AND D. N. EISENDRATH.

Before describing the tumor, extirpated by Dr. McArthur, a short review of our present knowledge of this form of neoplasm will assist in the comprehension of its peculiar structure. Prior to 1883, many forms of renal growths were grouped under the head of Lipomata. Some authors, e. g. Klebs[1], Sturm[2], Sabourin[3], had previously, and others at about the same time; e. g. Weichselbaum and Greenish,[4] described these neoplasms as adenomata arising from the renal tissue itself. Grawitz[5] was the first to bring order out of chaos when he maintained that these growths formerly described as lipomata, in reality had their origin in the supra-renal tissue misplaced within the kidney. "The cells," he wrote, "contained fat globules, lay four to eight together and formed columns and were sharply demarcated from the surrounding kidney tissue by a capsule." His reasons for believing these to be of adrenal origin were: 1. The subcapsular situation where aberrant adrenal tissue is likely to occur; 2. the cells were quite different in form from the renal cells and contained fat globules

in large drops like fatty infiltrated liver cells; 3, the capsule and the arrangement of the tumor cells in rows, like the supra-renal cortex with preponderance of cells over stroma; 4, amyloid degeneration of blood vessels present in his case only in the adrenals. Others, like Chiari[6], Lubarsch[7], and many others[8] to [15] inclusive, supported Grawitz' views and added the following criteria: 1. The similarity between tumors of the adrenal body itself and these growths. 2. The presence of glycogen. 3. Staining of nucleoli by Weigert fibrin and Russell fuchsin methods common also to the cortex of supra-renal gland but not to renal epithelium or to the cells of renal adenomata. Sudeck[18], DePaoli[16], and Driessen[17] maintained that these tumors were true renal adenomata and for a time a bitter discussion ([30] and [31]) arose. The view of Grawitz has prevailed and has been confirmed by many writers (19 to 29 inclusive) in recent years. Whereas Sudeck has claimed that they arise from the renal tubules, Hanseman[32] and Hildebrand[33] say that they are perivascular growths, and hence of endothelial origin. It will be impossibele to go into detail in regard to these opposing theories. The origin of certain renal tumors from misplaced adrenal tissue is now generally accepted by the majority of pathologists.

The frequency with which portions of the supra-renal tissue are found under the true renal capsule and embedded in the renal cortex was found to be astonishingly great by Grawitz[34]—at times an entire adrenal, at others only a portion which contains all three layers of the supra-renal cortex, the zona glomerulosa, fasciculata and reticularis. As a rule the cortex only is represented in these accessory adrenals, but May[35] found both cortex and medulla represented in two cases. The accessory adrenals are found in all portions of the surface of the kidneys. Those deeper in the cortex are explained by the fact that when the lobules of the

foetal kidney are united in early life they are enclosed, and remain buried in one of the furrows, and thus in the renal cortex. Accessory suprarenals are found in many places besides the renal cortex, viz., near the free edge of the broad ligament, between its layers[36], between the solar and renal plexuses, in the ovary, testis, spleen, along the spermatic cord, and veins. According to Schmorl[37], they are found in 92 per cent. of all bodies. According to Janosik and others the cortex of the suprarenal gland arises from peritoneal epithelium, and the medulla from ganglion cells of the sympathetic solar plexus.

The aberrant adrenals may develop into simple hyperplastic non-malignant, or into malignant tumors. If the latter, the primary focus may be very small, as in a case of Strübing[38], and the metastases enormous in proportion. Their growth is, as a rule, slow, and unless transmission along the veins has occurred, give rise to but few clinical symptoms. Owing to the extreme vascularity of the tumor, extensive hemorrhages may occur, and all that is found will be a large cyst containing blood. Lubarsch[39] and others believe that the presence of glycogen in these tumors is of the greatest diagnostic importance, and can be found with the iodin, hematoxylin, and gentian violet methods. The fat contained in the cells represents a metabolic process, and such intracellular accumulations of fat are characteristic of normal adult adrenal tissue. Beneke[40] found that in one case he could see a transition of the tumor into a sarcoma by gradual changes in the form of the cells and the increase of chromatin in their nuclei. Askanazy observed a similar change. Horn[41] claimed that they may undergo a gradual transition into carcinoma. Which of these views is to be accepted depends upon the fact as to whether the adrenal cells are looked upon as epi- or endothelial. The cysts at times observed, especially in the periphery of these tumors are,

according to the investigations of Ricker and Kelly, to be looked upon as the result of dilated uriniferous tubules in kidney islets within the misplaced adrenal tissue. The cells of the tumor are generally polyhedral, but may be elongated or flattened by mutual pressure and contain fat. Besides the glycogen spoken of above (which does not occur in the normal adrenals, but in hyperplastic and malignant tumors of this organ) lecithin also occurs. To sum up, aberrant adrenal tissue may be present in various places, but especially in the kidney itself. It gives rise to simple hyperplastic and malignant neoplasms, which correspond in structure to adrenal cortex especially the zona fasciculata, but with less regular trabeculæ. They are extremely vascular, and hemorrhages into the tumor are common. They are distinctly encapsulated, and may cause metastases in lungs, liver, bone, and so forth, by transmission through the veins.

The extirpated kidney in Dr. McArthur's case measures 12¼x7¼x9 cm. The anterior surface shows only toward the hilus and upper and lower poles a resemblance to the normal external appearance of a kidney. The remainder is occupied by an irregular, nodular tumor, a portion of which is broken down and the capsule torn off. The nodules extend as much as one-half inch above the level of the external surface; on section they are yellowish in color and are continuous with the main tumor mass to be described.

On the posterior surface the appearance resembles more nearly the external appearance of the kidney, the lower portion yellowish, the upper mottled red and yellow. There are only two such nodules visible as are described on the anterior surface, which are present along the convexity. One of these projects three-quarters of an inch beyond the level, about the size of a walnut and on section it seems to be continuous with the main tumor mass. The other is about the size of a bean; on section it is seen to be distinctly encapsulated; it contains one small cyst and some yellowish pigmented masses and is distinctly separated from the surrounding cortical tissue of the upper pole at which both are situated. About the middle of the posterior surface is a cyst in the cortex projecting slightly above the level. It was ruptured during the operation and looks like a simple retention cyst. Section of the kidney in

median line shows that a tumor more or less circular in form occupies the center of the kidney. The dimensions of the sections are 7½ cm.x9 cm. The tumor is distinctly encapsulated, toward the posterior surface it has caused an atrophy of the renal tissue to such an extent that that which remains varies in width from a mere connective tissue capsule over the middle of the convexity, about one-sixteenth of an inch in thickness, to one-fourth of an inch at the hilum.

In the anterior half there is no trace of kidney tissue over the tumor.

At the upper and lower poles there remain portions of renal tissue; in these the relation of cortex to medulla appears normal; the tissue is extremely firm with well-marked glomeruli.

The tumor itself, as stated above, is distinctly encapsulated, easily separated from upper and lower poles of renal tissue, shows toward the periphery in what are apparently recent areas, a yellowish, more or less homogeneous structure, the nodules varying in size from a pea to a walnut, each separated from the other by septa, which arise from the tumor capsule. In one of the older areas is seen a distinct cyst the size of a bean; others show a trabeculated appearance, in the meshes of which is dark, clotted blood.

About the center of the tumor there is an area the size of a half dollar, pale yellowish in color, soft, broken down, evidently necrotic. The tumor also occupies the entire pelvis of the kidney, the only portion remaining of the same being a narrow channel at the upper and lower borders of the kidney about the size of an ordinary ureter, which join each other at the hilum, and which apparently collected the urine from the still intact upper and lower poles. The tumor does not extend into the ureter, apparently having pushed the pelvis before it in its growth. The microscopic examination of sections stained with Delafield's Hematoxylin and Eosin, shows: 1. In the youngest, most rapidly growing portions of the tumor, large, clear, polyhedral cells; in many the protoplasm is replaced by one or more large vacuoles which represent fat (washed out by the alcohol in the process of preparing the sections. Many of the nuclei have been pushed to the edges of the cell by the fat contained therein. The cells are more or less regularly arranged in columns which are separated from each other by delicate septa of connective tissue which passes between the individual cells, thus forming a fine reticulum in which they lie. In many places instead of the solid septa, one sees fine capillaries separating the columns. There seems to be no regularity as to the distribution of the vessels. In some parts they are separated from each other by double layers of cells, in others by large clusters. Along many of the septa, especially those which are formed by vessels, there is considerable free, blood pigment (hemosiderin). This small growth, just de-

scribed, is completely encapsulated. The capsule at no place shows any openings through which renal tissue has grown into the tumor as described by Ricker. The connective tissue of the capsule is directly continuous with that of the adjacent kidney stroma. The renal structures immediately around it show the effects of compression with consequent atrophy of glomeruli and tubules. Farther away the parenchyma shows a moderate degree of interstitial change. The intertubular connective tissue and that of Bowman's capsule, shows a distinct increase. The tumor itself bears a striking resemblance to the stratum fasciculatis of the normal adrenal. In slightly older portions of the growth, e. g., the yellowish areas at the edge of the tumor (Specimen No. 1) the cells show less vacuolation, the clusters of cells are much larger than in the portion just described. In places the cells are so closely packed together and irregularly placed with relation to each other and to the blood-vessels that the picture reminds one greatly of a sarcoma. According to Beneke, such a change was observed by him in one case in this class of tumors. I do not believe that one could say that such a change had occurred in our tumor, but that rather through rapid growth there was no longer any resemblance to the structure of the adrenal cortex in such portions. Here and there one sees cells with spindle-shaped nuclei which look like non-striated muscle fibers. Section No. 2, in which the hemorrhages can be seen with the naked eye, shows microscopically cavities which have no walls, but seem to be spaces between cells of the above described type and arrangement, and which have been produced by mechanical separation of the cell groups. In these older portions there are cross-sections of large blood-vessels, and the cells seem to arise from the vessel wall. Such pictures may have given rise to the description of some of these growths as perivascular sarcomas, if their origin from aberrant renal tissue is not followed from more distinct fields. Tests for glycogen were made according to the iodin method, and resulted positively. The method was as follows: Lugol's solution, 5 to 10 minutes; alcohol to one part, tincture iodine, and 3 to 4 parts absolute alcohol. Clear in oleum origanum cretici. Mount in oil. The glycogen is distinctly seen in the form of small granules and more amorphous larger bodies of a deep brownish color.

CLINICAL HISTORY AND OPERATION.

F. S., 47 years, Bohemian, married, collector by occupation, gave a history of pain in the right lumbar region of several years duration, but not of sufficient intensity to confine the patient to the house or bed. Blood appeared in the urine in the early part of 1896, and continued intermittently for several months. The pain was aggravated by exertion, also the hemorrhage. In August, 1897, exploratory operation was made and the right kidney examined: two pigmented areas 1 cm. in diam-

eter were found on the posterior aspect, which were more resistant than the rest of the kidney. Digital exploration of the pelvis found the walls slightly thickened.

No bad after-effects were observed except a small leakage of urine for three weeks through the track left by the temporary drain. The hematuria almost ceased except for the occasional appearance of blood at intervals of from one to three months.

Microscopical examination of the excised fragment resulted in the diagnosis of melano-sarcoma.

Six months after the operation a small tender tumor was found in the region of the appendix, but there was no fever. Two months later a nodule was felt deeply seated in the lower pole of the left kidney. During this time and the year following the patient was in good health with but slight emaciation.

On Feb. 25, 1899, there was found marked increase in the size of the right kidney, and a mass the size of a hen's egg was visible at the posterior end of the old cicatrix. The new growth was sensitive to the touch and pulsating slightly. The patient had lost 10 or 20 pounds, and blood was again present in the urine. The kidney and the tumor were removed by the transperitoneal route. The capsule had formed firm adhesions to the cicatrix posterior to the kidney and the tumor, necessitating the incomplete removal of the part of the tumor which had grown in the cicatrix. The patient left the hospital 31 days after the operation, to return for the removal of the neoplasm in the cicatrix later.

April 10, 1899

BIBLIOGRAPHY

1 Klebs' Handbook, Bd. i, Abth. 2, p. 614, 1876.
2 Arch. fur Heilk., Bd. xvi, p. 193, 1875.
3 Arch. de Physiol. Norm. et. path., Tome ix, No. 1, p. 97, 1882.
4 Wiener Med. Jahrb., 1883, p. 213.
5 Virchow's Arch., Bd. xciii, p. 39, 1883.
6 Zeitschr. f. Heilkunde, Bd. v, 1884.
7 Virch. Arch., Bd. cxxxv, 1894.
8 Wilfel: Inaug. Diss., Bonn, 1885.
9 Hollen: Inaug. Diss., Greifswald, 1890.
10 Ambrosius: Inaug. Diss., Marburg, 1891.
11 Deut. Arch. f. Klin. Med., Bd. xliii, p. 599.
12 Deut. Zeitschr. f. Chirurgie, Bd. xxviii.
13 Ziegler's Beitrage, Bd. ix, 1890.
14 Virch. Arch., Bd. cxxvi, 1891.
15 Virch. Arch., Bd. xcii, 1883.
16 Ziegler's Beitrage, Bd. viii, 1890.
17 Zeigler's Beitrage, Bd. xii, 1892.
18 Virch. Archiv., Bd. cxxxiii, 1893.
19 Ziegler's Beitrage, Bd. xiv, p. 133.
20 Virch. Arch., Bd. cxxxvii, 1894.
21 Ziegler's Beitrage, Bd. xviii, 1895.
22 Brit. Med. Journal, Feb. 8, 1896.
23 Erg. d. Allg. Path. (Lubarsch), 1895-6.
24 Virch. Arch., Bd. cxlii, p. 164.
25 Virch. Arch., Bd. cxliii, p. 273.
26 Virch. Arch., Bd. cxlv, p. 112.

27 Virch. Arch., Bd. cxlv, p. 467; (a) Phila. Med. Journal, Vol. ii, 1898; (b) Kelynack: Renal Growths.
28 Centralbl. f. Path., Bd. vii, p. 363, 1896.
29 Centralbl. f. Path., Bd. viii, p. 417, 1897
30 Virch. Arch., Bd. cxxxvi, p. 568.
31 Virch. Arch., Bd. cxxxvi, p. 293.
32 Deut Med. Woch., p. 52, 1892.
33 Arch. f. Klin. Chir., Bd. xlvii, p. 225.
34 Arch. f. Klin. Chir., Bd. xxx, p. 824, 1884.
35 Virch. Arch., Bd. cviii, p. 446, 1887.
36 Arch. f. Path. Anat., Bd. xcii, p. 11, 1883.
37 Ziegler's Beitrage, Bd. ix, p. 523, 1891.
38 Deut. Arch f. Klin. Med., Bd. xliii, p. 599.
39 Virchow's Archiv., Bd. cxxxv, p. 149, 1894.
40 Ziegler's Beitrage, Bd. ix, p. 440, 1896.
41 Virch. Archiv., Bd. cxxvi, 1891.

STONES IN THE OVARY.

EMIL RIES.

Calcification of entire ovaries, or, calcification, petrifaction or ossification of tumors of the ovary, has been described repeatedly in a more or less reliable way. What is to be described here under the name of "stones in the ovary," is a formation which does not comprise the entire ovary, and takes its origin in a normal component of the ovary. Modern European gynecologic literature, as far as I can see, with the exception of a short communication by Slavjansky, contains no notice whatever of these formations, while the American literature contains two papers about them, published in 1892 and 1893.

My observations were made on three cases seen in one year, two operated on by myself, and one for which I am indebted to Dr. Hektoen.

The first specimen was discovered during the pathologic examination of a pyosalpinx removed with the ovary. The patient was about 40 years old and had had several children. The history of her disease and the operation were those usual in pyosalpinx. Searching for possible ovarian abscesses in the specimen which had been hardened in formol, I unexpectedly met with

a body as hard as stone, which resisted the knife very energetically. The ovary was not enlarged, and contained a number of old, and one fresh, corpus luteum, the latter showing the yellow color of its peripheral layer most plainly. The hard body could be broken in two with a very strong knife, and included a cavity which contained a small amount of brownish substance. The hard cortex was as white as the surrounding ovarian tissue. One-half of the stone was carefully enucleated from the ovarian tissue, and thus a hemispheric body with a peculiar surface was isolated. This body measured 13x11x19 mm. The surface showed tortuous elevations between which furrows existed, the whole resembling the suface of the brain, not that of a mulberry (see below). Microscopic examination of the brown substance in the cavity showed pretty well preserved red blood-corpuscles and numerous beautiful crystals of cholesterin. The cavity was invested with a membrane which was intimately adherent to the cortex, while it was smooth towards the cavity. It could be detached only in small shreds. After decalcification, a small piece of the cortex was examined in teased specimens. These, as well as specimens of the membrane investing the cavity, consisted of fibers of a hyaline substance without nuclei and of an amorphous mass of detritus.

Dr. Hektoen's case, as far as we could learn, presented nothing extraordinary in its clinical symptoms, or in the course of the operation. The specimen shows a small hydrosalpinx without any peculiar macroscopic or microscopic appearances. The ovary, with a number of old corpora lutea, is attached to the occluded abdominal end of the tube. The inferior border of the ovary is torn, and a few shreds of tissue unite this tear with a body 30x20x15 mm. in diameter, which, apart from its size, resembles the stone described in the first case, in every detail. This stone is so hard that it can only

be opened with a chisel. It presents the brain-like convolutions of the surface, is of white color, and contains an empty central cavity of about 4 mm. diameter again invested with a membrane. The stone is almost as large as the rest of the ovary, and fits snugly into the tear of the inferior ovarian edge, so that it is plain that originally the stone was located in the ovary and was imbedded in ovarian tissue as the stone in Case 1. Microscopic examination of a decalcified piece of the cortex shows the same lack of structure as in the first case.

Dr. W. S. Haines, Professor of Chemistry at Rush Medical College, kindly made a chemical investigation of these two apparently rare formations. I wish to express my best thanks to him and submit his report here:

"The fragments of the two ovarian calculi which you placed in my hands have been submitted to qualitative analysis. Both are found to consist of a mixture of organic and mineral compounds. The former is composed chiefly of fibrous material with minor quantities of fat and cholesterin, while the mineral matter is made up of the carbonates and phosphates of calcium and magnesium, with unimportant traces of chlorides and sulphates, presumably of sodium and potassium."

The third case was obtained in one of my operations, a vaginal celiotomy which was performed on a multipara of 40 years for procidentia and adherent retroflexion of uterus and tumor of the right appendages. After luxation of the uterus I palpated the right appendages and found a very hard ovary imbedded in adhesions, and a small tubal tumor. After the adhesions had been broken up and the right appendages had been brought down into the vagina for inspection, it was seen that the ovary contained a stone which at one point reached the surface of the ovary, while the rest was imbedded in ovarian tissue. Pressing against it with the tip of the

finger I could enucleate the stone without hemorrhage. A shell of ovarian tissue was left behind. The tube of this side was a hydrosalpinx, the uterine end of which had become severed completely from the uterus and presented as smooth and round an appearance as the abdominal end (spontaneous amputation of the tube). The other side was normal, with the exception of a few strings of adhesions which were broken up. The entire posterior surface of the uterus was covered with numerous larger and smaller cysts resembling a bullous eruption. The contents of the cysts were serous. Recovery uneventful.

The stone removed in this case has the measurements 52x24x18 mm.; it shows the same brain-like convolutions of the surface as the first two cases. It is easily broken in two by strong pressure with a knife, and the shell proves to contain a large and small cavity, which communicate, one with the other, by a small aperture. The cavity of the stone contains pultaceous masses (cholesterin and detritus), and presents on its wall a few flat convolutions similar to those on the surface, but smaller and less prominent. After removal of the detritus from the cavity, a smooth membrane is seen investing the cavity, which is so firm that it can be detached to some extent without tearing, and holds the two halves of the stone together after the shell has been cut in two. The shell is from 3 to 5 mm. thick and presents, in the fresh specimen, a distinctly orange-yellow tinge. The shell is less hard than in the first two cases, the deposition of lime-salts being apparently less advanced than in the other cases.

After decalcification, some hyaline threads and detritus without nuclei can be seen. The investing membrane is examined in cut and teased specimens, without giving any results different from those obtained from decalcified portions of the shell, nor do stains produce any better pictures.

The cases recorded in the American literature are the following:

Bland Sutton (London, Eng.), Amer. Journ. Obst., 1892, Vol. 26. At the post-mortem of a woman who had died from cancer of the breast, an ovary with two hard nodules is found. The one is enclosed in a cyst and presents a tuberculated surface like a mulberry calculus from the bladder, the other is of irregular shape and firmly imbedded in ovarian tissue. Both concretions are of the bright yellow color so characteristic of the recent corpus luteum. When cut across, it is seen that the calcific matter is deposited in tissue resembling soft leather in consistence. In another case Sutton received a cystic ovary as large as a child's fist, which contained in its wall a calcified body of the size and shape of an almond. The body is of bright yellow color and can be cut with a knife like the concretions in the first case. It consists of dense tissue impregnated with lime-salts.

Sutton arrives at the conclusion that these bodies are calcified corpora lutea. The drawing contained in Sutton's paper is very diagrammatic; the tubercles of the surface are drawn but indistinctly.

In 1893, Whitridge Williams (Amer. Journ. Obst., 1893, Vol. 28) describes a case which he diagnoses as calcified corpus luteum. The ovary is 5 cm. long, 2.5 cm. thick. No adhesions around it. In its center is a hard mass, 12 mm. in diameter, of bone-like consistence. It consists, on section, of two portions, a soft pinkish central portion and a hard bone-like exterior which is 2 mm. thick, and of a distinctly yellow color. The central portion resembles a blood-clot in beginning organization. Decalcified sections stain poorly, but the hard exterior of the nodule stains readily with hematoxylin, and presents a more or less homogeneous granular appearance in which it is impossible to distinguish any sign of nuclei. This is surrounded by more or less

typical, ovarian stroma, which stains poorly. The soft center-portion of the nodule is composed of dense fibrous tissue which is very poor in cells. Between this and the decalcified portion, we see several layers of small cells which possibly correspond to the membrana granulosa, though it is impossible to state their origin with certainty. In all probability the specimen represents a calcification of the large cells which surround a ripe Graafian follicle, and which form the yellow margin of the corpus luteum, while the fibrous tissue in its interior probably represents an organized blood-clot.

Slavjansky (Virchow's Arch., Vol. 51, p. 470) reports the following case: The ovary of a woman 71 years old was covered with very numerous and thick pseudo-membranes, and contained a concretion the size of a hazel-nut, which could easily be enucleated from the surrounding tissue. The concretion is round, 1 cm. long and 8 mm. thick, and contains a cavity. The wall consists of two strata; one internal mass, 1 mm. thick, firm and stained yellowish-brown by the preservation in chromic acid, and an external stratum, less firm, 0.5 mm. thick, and partially destroyed. A cheesy substance fills half the cavity. Microscopically, the cheesy mass contains detritus and fairly preserved shrunken red blood-corpuscles. The inner layer consists of very thick, glistening fibers, and a small number of spindle-shaped cells. No epithelium on the inner surface. The outer surface shows a high degree of fatty metamorphosis of the numerous cells which are larger than white blood-corpuscles, as well as the delicate fibers which are observed between the cells in small numbers. The neighboring ovarian tissue is old connective tissue with enlarged blood-vessels.

Slavjansky considers this a corpus luteum which has undergone cystic degeneration, and after having existed a long time has undergone regressive changes with deposition of lime-salts. The marked development of

the yellow stratum, as it occurs only in the corpus luteum of the pregnant woman, points to a degenerated corpus luteum, not to any other cystic formation.

My three observations differ in some essential points from those of Sutton and Williams, while my first case resembles closely Slavjansky's case. The size of the stones is of lesser importance, as it varies in my own observations from that of a cherry to almost that of a hen's egg. The configuration of the surface seems to be of greater importance for the explanation of the origin of these formations. Sutton compares the surface with that of a mulberry calculus. This comparison holds good in my cases only on the cross-section, the exterior outline of which indeed resembles that of a mulberry-stone. But on examination of the surface, it is seen that elevations and depressions are not arranged as in a mulberry, *i. e.*, round elevations surrounded by furrows. The surface resembles rather the convolutions of the brain, or as Morgagni describes it in a case apparently belonging here (quoted after Williams), the folds of the intestines. The corpus luteum is usually said to resemble a frill on a cross-section, and a cross-section will look very much like a cross-section of a mulberry. But looking at the surface, we get a different impression. I have carefully enucleated a well developed corpus luteum from the ovary of Case 1, which showed the frill-like arrangement on the cross-section, and I find that the surface shows a configuration similar to that of the convolutions of the brain, or the coils of the intestines as they are seen on opening the abdominal cavity, not that of a berry. I consider this an important macroscopic sign.

The color of the stones was yellow in the cases of Slavjansky, Sutton, Williams, and in my Case 3, while this color was absent in my first two cases. So far as the yellow tinge is present, it speaks in favor of the origin of the stones in the corpus luteum. Where the

color is absent we need not deny this origin, as it is well known that the yellow tinge is wont to disappear in the usual retrograde metamorphosis of the corpus luteum (corpus candicans).

The stones vary in hardness, so that some can be cut with a knife, while others have to be opened with a chisel or a saw. This proves plainly that we have to deal with a tissue more or less impregnated with lime-salts, not with a deposit of salts in an empty cavity or in a fluid. It is not remarkable that the microscopic examination of decalcified pieces of the wall does not reveal any distinct structural picture, as the infiltration with lime-salts ordinarily takes place in tissues which have undergone degeneration, preferably hyaline degeneration. Another point in favor of the opinion that we have to deal with some tissue infiltrated with lime-salts, is given by the fact that in all cases, excepting one of Sutton's, the stones are in firm connection with the surrounding ovarian tissue, as I could observe particularly well during the operation on my Case 3. The intimate relation between the stone and the ovarian stroma is additional proof that the stone has its origin in a component part of the ovary, and is not a calcification of the entire ovary for which it has apparently been mistaken in some older cases referred to by Williams. The shell of ovarian tissue which surrounds the stone may be so thin that the stone pierces it at some points naturally with the most prominent parts of the convolutions, as was especially plain in my Case 3. Sutton's Case 1 forms an exception, as he says that the stone was located in a cyst. As, however, nothing is said about the wall of this cyst, it must remain doubtful whether he had to deal with a real cyst, or only a stone loosened from its surroundings.

After the stones have been cleft in two, the observation of the center gives various results. Sutton's drawing shows a small cavity which is not mentioned in the

description of the case. In Williams' case the stone contains a soft, reddish core. In Slavjansky's case and my three cases the stones are hollow shells which surround, in Cases 1 and 2, one simple cavity, while in Case 3 a cavity varying in width, or rather two communicating cavities, are observed. The wall of the cavity observed from the inner surface presents convolutions like those of the external surface, and like the inner surface of a corpus luteum. Besides, my cases show a membrane investing the cavity, which is in firm connection with the substance of the stone, and can be peeled off in small shreds. The wall is made smooth by this membrane, which follows closely the elevations and depressions of the convolutions. No epithelium could ever be found on this membrane. The membrane resembles soft leather very much. Sutton also compares the tissue containing the lime-salts with leather. However, neither Slavjansky nor Sutton nor Williams mentions this membrane.

The explanation of this membrane meets with no special difficulties if we reason as L. Frænkel does in a recent paper on corpus luteum cysts (Arch. f. Gyn., Vol. 56, 1898). The stones, as well as the cysts, described by Frænkel represent pathologic conditions of the corpus luteum at various stages of its retrogressive metamorphosis. Frænkel distinguishes three types of cysts.

Type 1: Innermost layer corpus luteum tissue (lutein cells).

Type 2: Innermost layer connective tissue.

Type 3: Innermost layer epithelium or endothelium.

All these types are produced by central softening of the corpus luteum at various stages of its metamorphoses. Type 2, with the innermost layer made up of connective tissue, is explained by central softening at a time when the stage of corpus fibrosum has almost been completed. In this stage the nuclei of the connective tissue have disappeared more or less. If infiltration with lime-salts

were to take place at this stage, a condition very much like the one in my three cases would obtain. Williams' case, with the core, consisting of dense fibrous tissue poor in cells, is very important in this connection, because it proves one point which is especially important with reference to Frænkel's work, namely, the fact that the infiltration with lime-salts is not necessarily dependent on the previous formation of a cyst. It is perfectly possible that the infiltration with lime-salts precedes the formation of a cavity, so that Williams' case possibly forms an early stage of such stones as were observed in my three cases. Softening of the core may occur in spite of the shell of lime-salts, if only this shell contains, as it did in our cases, sufficient remnants of organic tissue that the substance of the stone is not perfectly homogeneous. What we have to deal with, then, is the formation of a cavity in a calcified corpus luteum, not the calcification of a corpus luteum cyst.

Either one of these pathologic processes may occur, and we shall try now to find which of them can be supported by additional evidence.

The size of the stones is proof neither of the origin in a non-degenerated corpus luteum, nor of the origin in a corpus luteum cyst. Corpora lutea of the size mentioned occur, especially as corpora lutea vera. In my Cases 1 and 3, several pregnancies had preceded the operation; in Case 2, and in the cases recorded in literature, it is unknown whether pregnancy had preceded or not. But there are enlargements of the corpus luteum which occur without pregnancy, and lead to the formation of good-sized tumors which the older authors used to call "gyroma," on account of the convolutions of their surface. Through the kindness of Dr. Ludvig Hektoen, I have recently received such a specimen, which contains a tumor larger than a hen's egg, with convolutions of the surface. This tumor is surrounded by a layer of normal ovarian tissue about

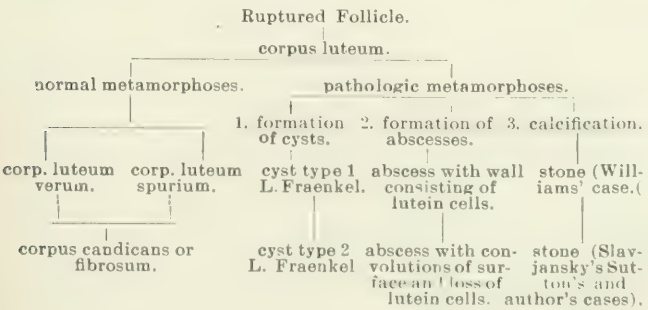
4 mm. thick. Sections of the tumor showed nothing but thick layers of lutein cells, some connective tissue and unchanged blood inside and outside the numerous capillaries present in the tumor. The case was therefore nothing but a hyperplasia of the corpus luteum.

The convolutions of the surface of the stones resemble exactly inside, as well as outside, those of the corpus luteum. Cysts of the corpus luteum show macroscopically (Rokitansky), as well as microscopically (E. Frænkel, Arch. f. Gyn., Vol. 48), the tortuous outline of the inner wall of their cavities. But outside, these cysts have a smooth wall, especially where they approach the surface; at any rate, they are less tuberculated than the stones are, even at the points where they reach the surface. This I consider a further point in favor of the opinion that the stones may take their origin in corpora lutea without preceding cystic degeneration.

The scanty contents of the cavities in my cases show nothing of importance. It might be important to find out which is the layer of the corpus luteum which undergoes the impregnation with lime-salts. But direct microscopic examination of decalcified pieces enabled neither Williams nor myself to arrive at the desirable certainty, as decalcified parts revealed no clear cellular structure. The examination of the tissue surrounding the stone revealed normal ovarian tissue. If some corpus luteum structure had been found, the layer which had undergone infiltration with lime-salts might then be found by a sort of subtraction. The fact, however, that the outlines of these shells resemble so closely those of the stratum of lutein cells, points strongly towards this stratum in its original or degenerated (especially hyaline) form as the seat of the calcification. It must be remembered here that after the disappearance of the lutein cells, the hyaline tissue of the corpus candicans keeps up the configuration of the lutein layer outside

as well as inside. As far as I know, no corpus fibrosum has ever been described containing a cavity at all approaching the size of those described here, while corpora lutea of this size, with a wall consisting of lutein cells, and a core made up of newly formed connective tissues, fibrin, and rests of blood, are observed frequently. For instance, the ovary of Case 1 contains such a corpus luteum the size of a cherry. Going from outside towards its center, we find in it a well-developed layer of lutein cells, then, first firm, then loose connective tissue, and in the center a fibrinous thready mass with some well-preserved red blood-corpuscles, as in the cavity of Case 1. Macroscopically, this fibrinous mass looks like a light jelly. Infiltration of the lutein cells with lime-salts would produce a condition very similar to that of the stone in the same case. Let us suppose that this jelly-like mass becomes a little more liquid, and we come to a point where it becomes impossible to say whether we have to deal with a soft corpus luteum, or with a corpus luteum cyst.

After all this we arrive at the conclusion that undoubtedly these shells can take their origin in simple corpora lutea, but that we can not entirely repudiate their origin in corpus luteum cysts. What has been said here concerning cysts of the corpus luteum holds good also with regard to abscesses of the corpus luteum, or suppurated corpus luteum cysts. The combinations of successive degenerative conditions may vary. It is possible to give a diagram of their development in the following way:


Ruptured Follicle.
corpus luteum.
normal metamorphoses.
pathologic metamorphoses.
1. formation of cysts.
2. formation of abscesses.
3. calcification.
corp. luteum verum.
corp. luteum spurium.
cyst type 1 L. Fraenkel.
abscess with wall consisting of lutein cells.
stone (Williams' case.)
corpus candicans or fibrosum.
cyst type 2 L. Fraenkel
abscess with convolutions of surface and loss of lutein cells.
stone (Slavjansky's Sutton's and author's cases).

As we have to deal here with shells in some connection with the ovum, the question of an atavistic formation might be raised, only, however, to be dropped at once, as the formation of the egg-shell is not a function of the ovary, even in birds. Lastly, there is absolutely no reason to believe in the origin of these stones in tumors—for instance—dermoids.

February 14, 1898.

CALCAREOUS DEGENERATION OF CORPUS LUTEUM CYST.

MAXMILIAN HERZOG.

The ovary was removed by Dr. F. Henrotin and consists of a fibrous mass, at one end of which is a calcareous globular body, the size of a large walnut. This calcareous mass is hollow, its hard wall being a few or several mm. thick. A microscopic study shows that the fibrous mass in some places contains tissue which still somewhat resembles ovarian stroma; well preserved follicles can not be found.

The calcareous mass externally is very uneven, it may in general be likened to a mulberry, though on closer inspection one sees that the depressions and protrusions more resemble the convolutions of a small brain than the surface configuration of a mulberry.

Pieces of the calcareous wall partly decalcified and sectioned show that the stroma or matrix consists of old fibrous tissue, mostly without any nuclei at all; only in a few spots could a scanty number of nuclei be found. The whole matrix is infiltrated with lime-salts; this infiltration is especially dense in the median zone of the wall.

From the character of the calcareous mass, its hollow

center, its convoluted wall, it appears that it is to be looked upon as a corpus luteum cyst which has undergone calcareous degeneration.

March, 14, 1898.

ON THE PATHOLOGY OF STUMP-EXUDATES AFTER SALPINGECTOMY.

EMIL RIES.

The usually smooth and rapid recovery of long series of patients after removal of the uterine appendages for inflammatory disease has often filled the laparotomists with proud satisfaction and the pleasant anticipations of having achieved permanent cures. Such anticipations have frequently been doomed to meet with disappointment. Schauta, for instance, reports (*Verh. d. Deutsch. Gyn. Ges.,* 1895), that an investigation of the remote results of his operations proved that no more than 56 per cent. of his cases were really cured, while the rest had more less troublesome symptoms. Chrobak (*Wien klin Wochenschr.,* 1893 and 1894) reports 67 per cent. of cures, while the rest of his cases were not much benefited by the operation. The causes of these unsatisfactory results are manifold. One of the most important causes—the stump-exudates—will find a new explanation in the observations which I shall lay before you.

Stump-exudates were found by Schauta (l. c.) in 28 cases out of the 172 salpingo-oöphorectomies. They have been found even more frequently by other observers and in my own experience I have repeatedly found them to be at the bottom of troublesome symptoms months after the operation. They occur bilaterally or unilaterally after bilateral or unilateral salpingectomy. They are observed immediately after the operation or they may originate a shorter or longer time after the operation.

They produce pain sometimes so severe that the patient is unable to attend to her work; in some cases the pain is even worse than it was before the operation. The exudates are found around the stumps of the removed tubes and vary in size from a barely palpable thickening of the uterine horn to the size of a hen's egg or larger.

As an explanation of the formation of these tumors Schauta (l. c.) offered the following two possibilities:

1. The inflammatory process creeps on through the uterine wall into the surrounding parametric and perimetric tissue; and

2. Germs were present in the broad ligament at the time of the operation (though no actual observations could be offered as evidence of this), the connective tissue of the broad ligament was laid bare by the operation, and in this way the germs could invade the peritoneum.

Though these explanations did not meet with any opposition, it can not be overlooked that we have no observations bearing out the correctness of these hypotheses. Besides, I can not help feeling that they are very artificial.

I had the good fortune of getting for microscopic examination three uteri which were removed months or years after one or both tubes had been removed. The examination of the tubal stumps in these cases, which was begun with a different object in view, gave results which, unexpected as they were, cast a strong light on the pathogenesis of the stump-exudates.

The cases are the following:

Case 1.—Mrs. J., twenty-four years old. Seven months previously a left pus-tube and ovary had been removed. A sinus remained which would not close. Besides, patient has an ovarian abscess the size of a fist and hydrosalpinx on the right side. Uterus adherent all over, forming part of the wall of the sinus. I operated September 28, 1896. Laparotomy. Removal

of ovarian abscess, hydrosalpinx, uterus, excision of sinus which leads toward the right crista ilei and terminates in an abscess which contains five silk ligatures. Recovery.

The stump of the tube which had been removed seven months previously is excised and examined in a series of sections embracing the entire stump up to the interstitial portion of the tube. The cavity is open throughout. The epithelium is the usual low columnar epithelium of this portion of the tube and stops at the surface of the stump without investing the cut surface of the stump. No threads to be found in the stump.

Case 2.—Miss W., twenty-five years old. Several years ago removal of both tubes and right ovary. Now chronic pelviperitonitis and adherent retroflexion. Operation by Dr. W. H. Rumpf, on December 8, 1896. Vaginal hysterectomy.

Both tubal stumps are examined in series. They are perfectly permeable, though the cavity is very narrow. Epithelium well preserved up to the abdominal opening of the stump. Besides, the left tube contains some epithelial ducts outside the circular muscular layer of the tube, one of which enters the circular muscular layer itself but does not show any communication with the tubal cavity (remnant of the Wolffian body). No threads to be found in the stump.

Case 3.—Mrs. H. Several years ago removal of both tubes and ovaries. Since then development of fibroids in the uterus; 1897, vaginal hysterectomy (Dr. F. Henrotin). Both tubal stumps are cut in series of sections and contain an open cavity clear up to the abdominal opening of the stump, the epithelium being well preserved. No threads to be found in the stumps.

The observation that the stumps of the tubes did not become occluded was somewhat of a surprise to me. I had expected to find the stumps impermeable, and I had never met in literature with any statement to the

contrary. The literature on this subject, however, is not at all extensive. The only statement I could find concerning the condition of the tubal stumps after salpingectomy is made by Gottschalk in a paper on castration atrophy of the uterus (*Arch f. Gyn.*, Vol. 53, 1897). Gottschalk reports that in a case in which the tubes had been removed on account of bilateral pyosalpinx in March, 1893, he had to extirpate the uterus in April, 1896, on account of exhausting watery discharge. In his description of the specimen we are interested in the following statement: "The tubal cavity shows mere agglutination and loss of epithelium just at the point of ligation. From this point to the uterus the tubal cavity has remained open. The uterine orifice of the tube was also open." Gottschalk does not state where the point of ligation was and what was the condition of the tubal cavity external to the point of ligation. It would be interesting to learn something about this point as well as about the method after which the salpingectomy was performed.

At all events, Gottschalk's communication proves that my observations must not be generalized without further investigations. The cases seem to differ. In some the tubal cavity becomes occluded; in others it does not. Presumably the technique of the operation has something to do with this difference, though at present we are not in a condition to say how much. If the uterine end of a tube is broken off in the course of the removal of a tube, as happens frequently in cases where the tubal tissue is chronically inflamed and infiltrated, it is often unnecessary to put any ligatures on the stump. In these cases there is a greater probability of the tubal cavity remaining open. I could not find out whether this occurrence had taken place in the three cases which I have reported above. Cauterizing the stump will hardly suffice to bring about complete occlusion. If the tubal stump is ligated with silk the thread remaining on the

stump for a long time may, by pressure atrophy, bring about complete occlusion, while catgut perhaps will be absorbed before pressure atrophy of the mucous membrane has been effected. Stitching the peritoneum over the tubal stump, or better even, excising a wedge of uterine tissue with the tube and closing the uterus with sutures through its muscular coat will most likely be the most efficient method of occluding the tube.

My observation that the tubal cavity may remain patulous after salpingectomy appears to give a simpler and more rational explanation of the origin of stump-exudates than any other theory hitherto offered. It is clear that the tubal lumen remaining open, infection ascending from the uterus, finds ready access to the peritoneum, through the open tubal stump, just as primarily the infection spreads from the uterus, along the tubal mucosa into the peritoneum. This latter process causes perisalpingitis, perioöphoritis, perimetritis, the conditions so frequently associated with tubal inflammation and a perisalpingitis forming around a tubal stump is exactly the condition which is clinically termed a stump-exudate. These observations explain also the difference between two classes of cases, one class being characterized by the occurrence of the stump-exudate during the convalescence from the operation, in the other class the stump-exudate occurring months after the operation. In the first class the infection has spread through the open tube from the uterus which contained infectious material at the time of the operation and could not be made completely aseptic. In the second class of cases the uterus has been healthy or was made aseptic at the time of the operation, but the uterus is infected and the infection spreads through the open tubal stump after the patient has left the hospital.

If, after removal of the tube its stump can remain open it is not only possible that an infection spreads through it, but an ovum may pass through the patulous

stump and pregnancy takes place. And, in fact, the modern literature contains a number of cases which are almost experimental evidence of the possibility of the tubal stump remaining after salpingectomy. Such cases are published in the Transactions of American Gynæcological Society for 1896, and in the *American Journal of Obstetrics*, 1897.

Case 1.—Gordon (Tr. Am. Gyn. Soc., 1896, p. 104). In March, 1894, as the author thinks, complete removal of both tubes and ovaries on account of menorrhagia and dysmenorrhea. Both ovaries were large and flabby; no other pathological conditions recorded. Menstruation continues June, 1895, last menstruation. March, 1896, patient delivered of a healthy child. Nothing is said with regard to the technique of forming a stump, except that the tube was ligated.

Case 2. Sutton (*ibid*, p. 109). October, 1892, removal of a multilocular ovarian tumor from right side, pedicle severed with thermocautery, ligature passed close to the uterine horn. Removal of a cyst from left side, pedicle severed with scissors, ligature same as on right side. The material used for ligature is not mentioned. June, 1894, patient confined of a boy weighing 10½ pounds. February, 1896, patient confined of a boy of 8 pounds. Nothing special is said concerning the tube, but, concluding from the usual condition of the pedicle of ovarian tumors, we must assume that the tube participated in the formation of the pedicle and was also removed.

Case 3 is described by Ill (*Am. Journ. Obstet.*, April, 1897, p. 532). December, 1894, removal of bilateral ovarian tumors. A small piece of ovarian tissue was left in the right stump. Twice afterward normal menstruation, then pregnancy and normal confinement. The author adds: "It must be apparent that the tube may slip from the constricting ligature and thus remain

patulous." He gives no detailed description of the technique observed.

It is worth mentioning that in the three cases quoted here the indication for the operation was not given by inflammatory disease of the tubes but by benignant tumors, therefore no formation of stump-exudate and the occurrence of pregnancy. If the tubes are removed on account of inflammatory disease the formation of stump-exudates will usually prevent pregnancy. That explains why pregnancy has never been described after removal of both tubes for inflammatory disease though of late it has become quite a routine practice to leave the ovaries if at all feasible.

A case which has some bearing upon the questions discussed here is published in a recent number of the *Centralblatt fuer Gynaekologie,* 1897, No. 40. Fritsch reports here that in a case of laparotomy for fibroid he enucleated the fibroid and then in order to make the patient sterile he put a silk ligature around the middle part of each tube without severing the tubes. Three years later the woman became pregnant and was confined normally. In this case Fritsch assumes that the thread cut through and a new communication between the abdominal and the uterine end became established at the point of the ligature. After the observations given above it must be regarded as possible that the thread cut through and a new orifice of the tube became established at the point of ligation, and that the ovule entered the tube at this point, not passing through the fimbriated end at all. After his experience with this case Fritsch has come to the conclusion that in order to make the patient sterile it is necessary to excise about one centimeter of the tube at a distance of about two centimeters from the uterine horn and to ligate the ends of the tube with catgut. I am afraid that this is no safer than his first method. My observations on the condition of the tubal stumps after salpingectomy tend

to prove that cutting and ligating the tubes does not necessarily bring about occlusion of the tubes.

This subject is apt to prove of some additional importance since Kehrer of Heidelberg proposed (*Centralblatt fur Gynaekologie,* 1897, No. 31) to make women sterile by cutting and ligating the tubes in cases where a future pregnancy is undesirable for some reason. As the new operation for vaginal celiotomy permits of very easy access to the tubes without making an abdominal incision this method of producing sterility may come into widespread use. I think it necessary to emphasize with special reference to my observations on the tubal stumps after salpingectomy that it is necessary to occlude the tubes by sewing the peritoneum over the stumps, or, better still, bringing muscular and peritoneal coats together. The suggestion of Beuttner, of Geneva (*Centralblatt fur Gynaekologie,* 1897, No. 40), is correct in this point, though I agree with him neither in his opinion that it is better to make an occlusion at the abdominal end of the tube instead of selecting the uterine end nor in his statement that the vaginal celiotomy does not give ready access to the abdominal end of the tube.

It is evident that the observations presented here have a very pronounced bearing upon the much-vexed question whether or not the uterus ought to be removed in every case in which the appendages have to be removed for inflammatory disease.

In conclusion, I have to express my thanks to my assistant at the Post-Graduate School, Dr. Gay K. Durbin, for aid given in the examination of these specimens.

November 8, 1897.

MALIGNANT PLACENTOMA.

JOHN MARSHALL BEFFEL.

The specimens that I have for demonstration to-night are of more than passing interest, first because of the rarity; second, because of the difficulty of diagnosing and naming the same. I believe this is the first original diagnosis and demonstration in Chicago of a specimen called by various names, as Deciduoma Malignum, Malignant Syncytioma, or Malignant Placentoma, and, unless I am mistaken, it is the second in the United States; the first in this country having been made by Williams of Johns Hopkins University in the fall of 1894.

It is not my purpose at this time to present an exhaustive paper on the subject of placentoma. All I wish to do is to demonstrate the specimens, and thus put the case on record. A more extended paper will be presented later.

The history of the case is as follows:

November 10, 1897, Mrs. Tilly W——, a Swedish woman 30 years of age, was admitted to the service of Dr. E. C. Dudley at St. Luke's Hospital. The following is the history of the case as shown by the hospital records.

Complaint.—(1) Pain over the right inguinal region. (2) Pain across lumbar region. (3) Headache. (4) Constipation.

Family History.—Negative.

Personal History.—Patient was married at the age of 22; she has had three children, the first child was delivered by forceps, the youngest child is three years old. In March, 1896, the patient had an abortion; at this time the uterus was curetted, and immediately following the curettement the patient had chills and fever, also hemorrhage from the uterus. This condi-

tion lasted for two months when she began to improve, except that her menstrual periods occurred every two weeks and she remained in a generally debilitated condition.

Present Illness.—Two days ago (November 8) patient had a chill and sudden pain in the right side which made her so faint and dizzy that she fell down but was not unconscious, she was nauseated and became tympantic. She had not menstruated regularly since July.

Dr. Dudley found a slight thickening of the right anterior uterine wall in the region of the right horn, but did not think the case one for operation. The diagnosis was pelvic cellulitis. After three weeks' residence at the hospital the patient was discharged.

February 9, 1898, the patient came to Dr. T. J. Watkins, who placed her in Provident Hospital. At this time a large tumor was diagnosed in the uterus and one in the region of the right lobe of the liver. February 12th, Dr. W. E. Schrœder performed an exploratory operation, finding a tumor the size of a large orange developing from the lower wall of the gall-bladder. A tumor of about the same size was found in the region of the right horn of the uterus. A diagnosis of sarcoma of uterus with metastases was made, and the case considered inoperable. A small piece of the tumor of the gall-bladder was removed for purposes of diagnosis, marked hemorrhage followed, and in spite of all attempts to check the hemorrhage by packing, by Paquelin cautery, etc., it continued, and the patient died within twenty-four hours.

The autopsy was performed by Dr. Frank X. Walls, demonstrator of pathology at Northwestern University Medical School, by whose kind permission I was permitted, upon his departure last March for Vienna, to make a study of the specimens, and to demonstrate the same when I made my diagnosis. Dr. Walls found the two tumors above mentioned, besides one small tumor in

the lower wall of the liver, and several small tumors in the superior lobe of the left lung. The kidneys appeared normal, microscopic sections did not reveal tumor tissue. The inguinal glands were normal. The mesenteric veins appeared thrombotic. Pieces were removed, but upon sectioning we found them free of tumor tissue.

The uterus and appendages were removed, as was also the right lobe of the liver, together with the tumor in the wall of the gall-bladder.

Gross Appearance.

The uterus is considerably enlarged; the left half almost normal, the right, both anterior and posterior, is markedly involved; its surface is nodulated, the right tube is almost hid from view by the extension of the tumor between the folds of the broad ligament. On cut section through the posterior wall we observe that the left uterine wall is of about normal thickness, the right wall is considerably thickened. The uterine mucosa is, as far as appearance is concerned, normal, except for an area about one centimenter in diameter lying near the right anterior portion of the fundus. Here the mucous membrane is broken and a mass projects slightly into the uterine cavity. If we continue the incision through the anterior wall we get a section of the tumor which appears red and spongy; it is not tough and fibrous, but rather friable.

The ovaries, so far as the tumor is concerned, appear normal, and microscopic examination of the right ovary shows absence of tumor tissue. The left ovary is cystic. There are three small cysts developing from its surface. They are probably oöphorotic cysts.

The gall-bladder.—Here we find a tumor about the size of a large orange developing in the lower wall of the gall-bladder. When sectioned it presents the same appearance as the uterus, except that this tumor is more friable, crumbling whenever handled.

The liver.—Near the border on the under side, close to the transverse fissure, is a tumor about three centimeters in diameter; it shows the same structure as the other tumors.

The lungs.—Several small tumors were found in the superior lobe of the left lung.

Histological Structure.

I will first describe the tumor in the gall-bladder, as this is least modified by the host.

First.—We observe the great amount of blood in the tumor; it looks in places like a hemorrhagic mass which has undergone partial coagulation and is crossed in all directions by fibrinous bands. In other places it lies in intimate relation with the characteristic cells of the tumor.

Second.—We note the presence in the blood-spaces of peculiar "long, narrow, wormlike bands of protoplasm," which contain many nuclei. The protoplasm of these masses is undivided, there being absolutely no trace of cell division. These syncytial masses present fantastic shapes. The protoplasm has a marked affinity for eosin, which is manifest if we compare its staining qualities with the red blood-corpuscles which have quite an affinity for eosin, the protoplasm being stained much deeper. The nuclei are quite large and irregular. They have a large amount of chromatin, and take up the hematoxylin stain very deeply. There is another characteristic of the protoplasm, namely, to be vacuolated. These vacuoles are often quite large and are found filled with blood. This may be due to the intimate relation which the syncytium bears to the blood-spaces; one side of the syncytium is always in contact with the blood.

Third.—We also note the presence of another set of cells, grouped irregularly and lying next to the syncytial masses. These cells have large round or oval nuclei which take the hematoxylin stain less readily than the nuclei of the syncytium. The nucleus is large

in proportion to the amount of protoplasm. The protoplasm of these cells does not stain as readily with eosin as that of the syncytial masses. I believe these are epithelial cells. Nowhere is there a connective-tissue stroma.

A section of the tumor in the lung shows a large vein which contains an embolus composed of typical syncytial masses embedded in a mass of fibrin, and lying loose in the lumen of the vessel. This shows beautifully how metastases occurred in this tumor.

A section of the uterus at the point where the tumor invaded the uterine cavity does not give us the typical picture described above; we do, however, find the syncytium in the venous spaces in the muscularis; but nowhere do we find these cells in the muscularis—they are always in blood-spaces.

The large cells which we find in the muscularis, and which take up the eosin stain deeply, are, I believe, degenerate decidual or connective-tissue cells, and are not to be confounded with the syncytium—while these cells are quite numerous, they hardly form an important part of the tumor.

Histogenesis.

1. There can be but little doubt that the tumor we are demonstrating originated in the placenta.

2. The blood-spaces may be a reproduction of the intervillous blood-spaces of the placenta.

3. The syncytium has its origin in the placental syncytial masses. We, of course, can not at this time go into a discussion of the histogenesis of the syncytium; most of the authorities agree, however, that they arise from the ectoblastic layer of the placenta—although this has not yet been proved.

4. The large epithelial cells, I believe, have their origin in the ectoblastic cells of the villi of the placenta.

Diagnosis of Specimen.

We will note the following facts:

First.—The development in the uterus of a tumor following an abortion is a suspicious circumstance.

Second.—The history of the rapid development of metastatic tumors in a little over three months shows the marked malignancy of the tumor.

Third.—The histological structure of syncytium, ectoblastic cells, and blood-spaces, constituting the microscopic symptoms of the tumor, when combined with the above history, leads us to a diagnosis of malignant placentoma.

Differential Diagnosis.

This specimen has been diagnosed as giant-celled sarcoma. That there are giant cells here there can be no doubt; there are not, however, myeloblastic cells. There were no lesions present in the bones. In myeloid sarcoma we usually have a dense stroma made up of spindle and round cells. There is positively no connective-tissue stroma or matrix in this tumor. The myeloid cells do not, as a rule, branch as do the syncytial masses here.

It has also been diagnosed as angiosarcoma. The presence of large quantities of blood in a tumor does not make it angiomatous. The blood in this tumor is not confined in blood-vessels, but is held in by the syncytial masses, together with the ectoblastic cells forming these blood-spaces. Nowhere do we find these spaces lined by endothelium. We do not have the cells arranged in stratified layers about the blood-vessels as in angiosarcoma.

I think it is not deciduoma malignum, which is, as its name signifies, a malignant tumor, the main cells of which are the cells of the compacta of the decidua serotina, or the decidual cells. The uterine tumor alone suggests this diagnosis. The cells in the muscularis which appear as decidual cells are not in a state of rapid proliferation, but rather in a degenerating state. The masses of cells lying next the muscularis or in the

venous spaces I believe to be the ectoblastic plates described by Siegenbeck Van Heukelom, in the *Archiv. fur Anatomie und Physiologie* for 1898, in an article on human placentation.

I believe the decidua is not involved in this case. The tumor has been called a carcinoma because it is believed that the syncytium and the ectoblastic cells, or cells of Langhans both have a common origin, namely, the epiblast or outermost layer of the germ-vesicle. If this is the correct histogenesis of these syncytial masses, then this tumor is a carcinoma and not sarcoma. The union of these two forms of cells in the metastatic tumors rather leads us to believe they have common origin.

You can see that the naming of this tumor depends not upon the pathologist, but upon the embryologist. There are four theories for the origin of the syncytium:

1. From the endothelium of the blood-vessels. 2. From the uterine gland structure. 3. From the compacta of the decidua. 4. At present the most generally accepted theory is that the syncytium arises from the ectoblast. But until the embryologist has proved the origin of these masses, I prefer the name malignant placentoma, or malignant syncytioma, although the latter term does not indicate the presence of the blood-spaces or ectoblastic cells.

June 14, 1898.

STUDY OF AN EARLY PLACENTA *IN SITU* OBTAINED FROM THE LIVING.

MAXIMILIAN HERZOG.

The observations to be reported in the present paper were made on a comparatively young placenta *in situ*, obtained under such favorable circumstances as to ex-

clude with absolute certainty any and every post-mortem change. For the valuable specimen which forms the basis of this investigation I am greatly indebted to Prof. James H. Etheridge.

The history of the case as far as it is necessary to refer to it is briefly as follows:

On a young, respectable, unmarried woman, not suspected of pregnancy, a laparotomy for the removal of multiple subserous myomata was made by Dr. James H. Etheridge at the Policlinic Hospital. When the uterus had been severed by a circular incision well down in the upper part of the cervix, and had been removed, part of a small bald bladder presented in the opening created by the amputation.

The specimen, as removed, was sent at once from the operating room to the pathological laboratory, with the request that I should open what appeared to be an ovum, to see whether it really was one, and whether it contained a normal embryo. The bladder, was, however, not opened, but, on the contrary, left entirely undisturbed, and the specimen as removed was immediately placed in a large quantity of alcohol and formalin to fix and harden it as a whole, without disturbing the relation of the parts, or giving rise to any change of pressure of the fluids contained in ovum, placenta and uterus. After being hardened in alcohol and formalin, the ovum, for such it proved to be, was opened and the specimen examined, the following being the main features of the inspection:

There is springing from each side of the uterus a subserous myoma. Both myomata have a direction upward and outward from the median line, forming together at their attached bases an acute angle. The larger left myoma measures from base to apex about 13 c.m.; the smaller, left, one 9 c.m. The uterus itself, mostly hidden from view, seems to be enlarged two or three times its normal non-pregnant size. Its wall ap-

pears considerably thickened. The ovum, which protrudes from the uterus, has a largest diameter of from 7 to 8 c.m. The placenta, which is almost circular, has a diameter of 5 to 6 c.m. The cord is inserted markedly eccentrically, about 5 c.m. long, 2½ to 3 mm. in diameter, and shows 8 to 10 turns.

The embryo itself is 1-2 mm. less than 5 cm. (Steiss-Nackenlænge) long. The head forms more than one-third of the total length and more than one-third of the bulk. Legs and arms are both flexed at nearly right angles to the body, the hands touch the upper part of the face and the lower part of the frontal region. In other words, the position and configuration of the embryo is such as is normal at the stage of development represented. The external genitalia seemed to indicate the male sex, yet there is still a slit-like opening under what is probably the penis, but what might be the clitoris.

The embryo, as a whole, is round and plump, well-shaped, the skin is in very good condition. Every feature of decay, maceration or compression is absent from the fœtus.

The age of the embryo, I think, is from nine to ten weeks, nearer probably to the former than to the latter period of time.

After the specimen had been hardened *in toto* cubical pieces from 1 to 1½ c.m. long were cut out from the margin of the placenta, as well as from a central place near the insertion of the cord (including part of the muscular coat of the uterus). Also pieces from the membranes near the placental margin, and from the antiplacental pole of the ovum. These pieces of tissue were dehydrated in absolute alcohol, and subsequently embedded in paraffin and in celloidin. The stains employed for the study of the sections were hematoxylin and eosin, borax-carmin Van Gieson st., and Weigert's fibrin st. Besides, embedded as well as non-embedded sections were examined for hæmosiderin and hæmatoi-

din by the usual micro-chemical methods (hydrochloric acid; ferrocyanide of potash; sulphuric acid).

A considerable number of sections were examined, among which series of respectively 72, 50, 40, 28 and 24 sections of 20 mm. thickness, thinner sections were made for studying individual cells.

The literature upon the human placenta is such a voluminous one that I must in this paper refrain from referring to it in full, stating, however, that in two of the very best monographies which we possess upon the subject—those of Minot[1] and Waldeyer[2]—one may find full references to the numerous and often very contradictory writings concerning the placenta.

This subject has also been very thoroughly considered upon the basis of the work of others, as well as upon numerous personal observations by Webster[3], in his excellent book on "Ectopic Pregnancy[4]." Proceeding to the minute description of our specimen, it is the *amnion*, the innermost of the fœtal membranes which first engages our attention. It is derived from the extra-embryonic somatopleure and consists, therefore, of an inner layer of ectodermal tissue (epithelium) and an outer layer (looking toward the chorion) of mesodermal tissue.

Minot, I think, has furnished the most extensive and best description of the amnion, which I can affirm in its main features. My sections show the amniotic ectodermal epithelium as a somewhat irregular layer, the cells are so arranged that it might be said that they form two incomplete layers mutually infringing upon each other, rather than one well-defined, regularly arranged single layer. At least, this description is true for many places. In others, again, the epithelial cells have, as it seems, become flattened by pressure so as to form a more uniform single row. There is to be seen in many places the clear cell-free space previously described by Minot. It ought to be mentioned that the epithelium

is evidently only very loosely attached to the mesodermal layer, because it is very easily stripped off, missing, therefore, in most places, or presenting itself as detached. The nuclei of the ectodermal amniotic epithelium are vesicular oval bodies showing an intranuclear network. They stain fairly deeply with nuclear stains, though not as intensely as the nuclei of the mesodermal cells to be mentioned presently. The cell protoplasm of the amniotic epithelium is finely granular and very distinctly vacuolated, and the cells are con-

Fig. 1. (Leitz obj. No. 1; eye-piece No. 3.) a. Amnion; b. Cavity in amnion containing degenerating cells; c. Chorionic space (space below chorion and amnion); d. Chorion with two blood vessels and one villus; e. Intervillous space; f. Villi cut transversely

nected with each other by intercellular bridges. Attention has been called to this by Minot, who gives (l. c.) a picture of these cells. In my sections, however, the vacuoles are decidedly smaller than they are pictured by Minot. The intercellular bridges, I find, likewise, finer and more numerous. I agree with Minot (against other views expressed) that these intercellular processes are truly protoplasmic and not processes of a cell membrane. I think, however, that there is a certain moderate but still striking similarity between these ectodermal amniotic cells and the prickle-cells found in the Malphigian layer of the adult epidermis.

The mesodermal connective tissue (mesenchyma) forming the bulk of the amnion, is of a type which is perhaps best characterized briefly as a very young embryonic connective tissue of an abundant homogeneous stroma or matrix, in which are embedded cells with deeply staining oval, fusiform, or somewhat irregular nuclei. These cells possess mutually intercommunicating processes; they are suited in lacunæ, in vacuolated spaces in the homogeneous matrix.

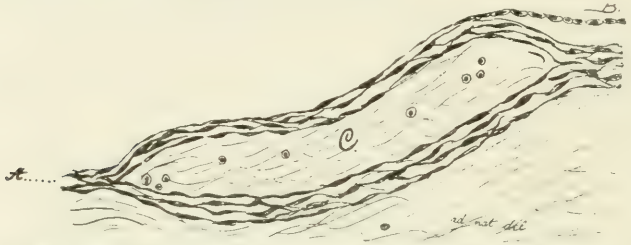


Fig. 2 Cavity in amnion containing degenerating cells. (Leitz obj. No. 7, eye-piece No. 3.) A. Amnion single layer: b. Epithelium lining amnion: c cavity contained between two layers of amnion.

Near the insertion of the umbilical cord I found the following condition, which I think has not been noticed before: The membrane becomes somewhat thickened in places and then splits up in its middle into two layers. These two layers enclose a cavity. That this split is not an artefact is proven by the following: Where the split has occurred there is usually a marked thickening of the membrane. The open cavity is bounded by fusiform connective tissue cells which form a complete flat lining. There are contained in these cavities of the amnion a number of degenerating cells, which are large and round, showing the features of hydropic swelling. Their nuclei stain very dark, they are granular, not vesicular, and indistinct in outlines.

The description as given so far refers to the placental amnion. At the antiplacental pole of the ovum, the ectodermal epithelial cells were almost entirely missing, in many sections only a few flattened ones being found

occasionally. The mesenchyma presents itself as a tissue composed of very much flattened wavy cells and fibers. Between this condition and that found opposite the placenta there is a gradual shading off as one goes from the antiplacental region to that of the placenta. At the latter amnion and chorion are still perfectly separate, being, as it seems, held apart by a small amount of fluid (chorionic fluid). The more one moves away from the placenta, the more closely the amnion approaches the chorion, and at the antiplacental pole the two membranes are so completely fused that the boundaries have become entirely obliterated. At the placental site, the amnion at its outer (chorionic) side possesses a distinct lining composed of a single layer of fusiform cells, but whether these latter are to be looked upon as a condensed mesenchymal, or as a mesothelial layer, could not be decided in this case. The *chorion* from its development, is defined by Minot as "the whole of that portion of the extra-embryonic somatopleure which is not concerned in the formation of the amnion." Looking at it as a complete organ, after it has closed around the embryo and amnion, we may describe it with Schaefer[5] as that external membrane of the ovum from which the villi spring.

The chorion is developed from the amnion by a reflection of the latter, before it has closed completely over the dorsal surface of the embryo. The chorion, therefore, consists of an inner layer of mesodermal connective tissue and an outer layer of ectodermal epithelium.

While at a very young age the mesoderm of the chorion and that of the amnion are very much alike, in the placenta under discussion the mesoderm of the chorion frondosum,— *i. e.*, the placental chorion—is markedly different from the amniotic mesoderm.

Embedded in a homogeneous matrix we find decidedly fusiform cells with nuclei of a similar shape. These

cells are arranged in parallel rows, their bipolar, filamentous processes being slightly wavy. The matrix in which these cells are situated is vacuolated like the amniotic stroma, but it seems that the vacuoles do not surround the cells, but are almost without exception found on one side of the cells.

The stroma of the chorion at the non-vascular areas is about two to three times as wide as the amniotic mesoderm. At the vascular parts it is, in consequence of the bulging of the blood-vessels, very much thickened, and frequently six to seven times as wide as the amnion.

The blood-vessels are comparatively thin-walled and simple. They show an internal endothelial lining, and around it from one to three rows of concentrically arranged fusiform cells with fusiform, or rod-like nuclei, having to all appearances the character of involuntary muscle fibers, though they are by no means as characteristic as these cells found in an adult medium-sized blood vessel. Around the cells just described there is a moderate condensation of the chorionic mesoderm.

The ectodermal epithelium of the chorion may conveniently be considered with the same structure of the villi. Where a large villus arises from the chorion the mesoderm changes somewhat in character. The cells become more complicated, instead of being simply fusiform, they become more or less stellate, and the intercellular vacuoles become very much larger. In a cross section of a larger villus the mesoderm may be described as follows: Most of the cell nuclei present themselves as fusiform, or rod-like vesicular bodies. They stain fairly deep, showing a reticular network. Around the nucleus there is found a finely granular protoplasmic cell body which sends out processes. These processes seem to interlace with each other, and the network so formed incloses numerous vacuoles, often as large as from six to seven times the diameter of a cell body. These vacuoles are undoubtedly filled with some fluid,

they are therefore true "Safträume." Besides the cells just described, there is another type to be found in the core of the villi, viz., cells with a perfectly round vesicular nucleus, with a large spherical zone of finely granular cytoplasm. These large round cells do not possess any processes. The larger blood vessels found in the larger villi are identical in their make-up with the blood vessels found in the chorion. Before entering upon the description of the epithelium[6] of chorion and villi it should be stated that some observers have claimed that this epithelium rests upon a well-differentiated basement membrane proper. I think that from the study of my specimens I can deny this claim unconditionally. On the chorion frondosum the epithelium rests directly upon the mesodermal tissue described above, the cells of which toward the epithelial lining have undergone a slight condensation, but it can in no way be said that a true basement membrane is formed. When the large villi arise from the chorion, even this slight condensation of the mesoderm disappears, so that there is absolutely nothing left to indicate a basement membrane. On the cross-sections of the villi it can often be seen how the core of the villus, in consequence of the process of hardening, has retracted away from the epithelial covering. The core then often appears very sharp in outlines, because the united cell processes described previously form a well-marked external boundary line of the core. This arrangement must, I think, have been mistaken for what has been described by some investigators as the basement membrane of the epithelium of the villi.

The Epithelial Covering.—The epithelial covering of chorion and villi, which has been the subject of so much discussion, speculation and interpretation, in my specimens everywhere presents itself as a very distinct double layer. The inner layer, now generally known as the "Langhaus Zellschicht," consists of a single row of cells.

the outlines of which can, as a rule, be easily made out. Some observers have denied that in the inner epithelial layer the cell boundaries can be well distinguished. This, as far as the placenta under discussion is concerned, is certainly not correct. Of course, the cell outlines and boundaries are not as distinct as those of decidual cells, for instance, but they are distinct enough to be fully appreciated in favorable places. The cells of the Langhaus layer are cuboidal and sometimes short columnar, one axis being sometimes markedly longer than the other one. The nuclei are vascular, of round or oval shape. The boundaries of these cells I have best seen in medium-sized villi and in the short columnar type. I have not been able to find in my sections that the cells of the Langhaus layer do, as has been claimed, present themselves sometimes as a double or triple layer.

The outer epithelial layer, the *syncytium* or plasmodial layer, does not show any cell boundaries at all. It forms a continual nucleated plasmodial band or mass on the outer surface of chorion and villi. The nuclei of the synctium are, as a rule, somewhat smaller and more oval than those of the Langhaus layer. They are very densely packed side by side in the plasmodial strip. So densely are they frequently found that even in thin sections one often sees that they overlap each other. I cannot find that the syncytial nuclei are so very much richer in chromatin than the Langhaus layer nuclei, as has often been remarked by writers upon the subject. They are somewhat richer in chromatin, but the difference is certainly not so great as has been emphasized, probably, I think, on account of the fact mentioned, that the plasmodial nuclei often overlap each other, and then, of course, appear darker at such places where this is the case. The chromatin in both types of nuclei (Langhaus and Syncytium) shows itself in the shape of granules. The picture of a well-marked intranuclear network I have not been able to observe.

At many points of the chorion the plasmodial layer sends out buds composed of syncytium only. These buds rarely, but sometimes do, arise at right angles, as a rule, at an acute angle; sometimes they stretch out almost parallel to the surface from which they spring. These plasmodial buds are looked upon as the first stage of a new complete vascular villus, which, as is well known, form throughout almost the entire term of pregnancy. Such plasmodial buds also arise from the larger villi. The are quite numerous in all of my sections, and they have frequently been severed completely from their mother villus by the direction of the cut. They then appear to float as free islands in the intervillous space. They are, however, in reality not free islands, as can be easily demonstrated on serial sections. Some of the syncytial buds in section appear completely solid, others contain a hollow canal in the middle, others, again, are irregularly evacuated. Where villi have become adherent to the decidua, a condition frequently found, this attachment is brought about by the syncytium. Its mass covering the villus at such a place has become greatly enlarged by proliferation of the nuclei and increase of the plasmodial substance. This tissue, which, it seems, does not contain any other elements but syncytium, forms the connective substance between the villus and the decidua. These plasmodial masses are found projecting preferably into recesses and depressions of the decidua, but they also spread out in a flat manner over even decidual tissue. It can always be noticed that wherever a plasmodial strand connects a villus with the decidua, the syncytium spreads out to a larger or less degree, and sends processes, as it were, over decidual surface. I am, however, certain that in my specimens the decidua serotina is *not completely* lined by a layer of syncytium. Occasionally it can also be seen how a plasmodial mass has penetrated into a maternal blood space, and has become attached to its wall. I may here

mention those islands found in the intervillous space and called "zellknoten" (cell nodules) by Kastchenko. They are, as can be demonstrated in serial sections, no islands at all, but only pieces of decidua on which plasmodial masses had fastened, or into which these masses penetrated to some extent. They have, in consequence of the direction of the knife, become severed from the decidual hills, and therefore appear in sections, as islands floating in the intervillous space, similar to the apparent syncytial islands mentioned above.

The chorion at the antiplacental pole still shows numerous remnants of villi, and in some the epithelial covering can still be recognized to a certain extent. The degenerated villi are small in size, do not show any blood vessels, and are of course, directed toward the decidua reflexa. The chorion at the antiplacental pole consists of wavy fibres of the same character as those before described in the amniotic mesoderm at this site. There is here no difference between the mesoderm of these two membranes, which are, as stated before, so intimately blended that no distinct boundary line can be made out.

In the *decidua serotina* we find the outer or compact layer best marked in the *middle of the placenta,* near the insertion of the cord. Toward the placental margin the compact layer becomes less and less marked, because the whole of the serotina, which here loses in diameter, is broken up by blood sinuses and enlarged gland spaces, so that it might be said that here we have only a spongy and no compact layer at all. Where the compact layer is well developed it shows those projecting hills so well described by Waldeyer. As remarked before the adherent villi, the "haftzotten" of the German writers, are frequently seen inserted in the valleys and clefts between the elevations of the compacta, but also adherent to, or near the summits or to the sides of the hills. The compacta of the serotina is composed of those very large cells known generally as decidual cells. They are in our

case perhaps not so beautiful in the serotina as they are found in the vera. However, a description of them may be given at this point. The *decidual cells* are generally more or less oval or fusiform in outlines; some seem to be almost spherical. Their protoplasm is finely granular, and one occasionally sees processes connecting neighboring cells with each other. The cell boundaries are very sharp; in fact as sharp a boundary is perhaps rarely seen in any other kind of cells. This, it appears to me, is due to the fact that the decidua possesses an unusually large amount of a homogeneous intercellular substance. The nuclei are large vesicular bodies, round or oval, poor in chromatin, and show very distinctly the nuclear membrane. The great majority of these cells contain one nucleus only, some two, few three nuclei. More than three nuclei in a decidual cell I have not found. The multinuclear giant cells, said to be found during the more advanced period of pregnancy, I have not seen in my sections. A second kind of cells is found wherever we have decidual tissue, viz., small, round cells, which I will call leucocytes, though I am not certain whether they are, or whether they are connective tissue corpuscles, the so-called "wanderzellen" of the connective tissue. The leucocytes are, of course, very easily recognized in decidual tissue, as they are so very much smaller than the decidual- cells proper. These leucocytes, which may be seen anywhere in decidual tissue, are greatly increased at the margin of such places where the decidua is showing necrotic changes. This condition is already found extensively in the serotina of our placenta. In such places the decidual cells have almost completely disappeared, or we only find non-nucleated, poorly defined cell remnants; the tissue has become more or less completely structureless and uniformly homogeneous and hyaline. Around such decidual tissue showing the evidences of coagulation necrosis, there is an abundant

accumulation of leucocytes, with deeply staining granular nuclei. Quite a characteristic feature of this small, round cell infiltration is the fact that many nuclei are found in the process of nuclear fragmentation. I think that this picture misled Eden[7] to assume that the decidual cells themselves disappear by becoming smaller and by finally undergoing nuclear fragmentation.

The picture furnished by the leucocytes in the process of nuclear fragmentation found in connection with degenerating decidual tissue is so highly characteristic that it has served me to recognize otherwise entirely changed decidua, as it is frequently found in the blood coagula formed after rupture or abortion in ectopic pregnancy.

If a theoretical consideration be permitted, it may be stated that the finding of necrotic places in the serotina of the early placenta strongly favors the view that the main physiologic function and importance of the decidua is limited to the very earliest term of gestation only. After the formation of the intervillous space and the establishment of the fœtal circulation in the chorionic villi the human decidua, as far as the nutrition of the embryo is concerned, only plays a very unimportant rôle, or none at all.

Under the compact layer we find in the decidua the *spongy layer,* showing many and large open spaces. These latter are enormously enlarged uterine glands. In the spongiosa of the serotina of our specimen these gland spaces have no connection with the intervillous space. In the formation of the decidua serotina, it appears to me that the original openings of the glands become at a certain time obliterated or closed, in consequence of the proliferation of the decidual cells. The deeper and very much enlarged parts of the uterine glands become the gland cavities in the spongy layer. They are, in our specimen, of oval outlines, sometimes very long clefts, partly lined by epithelium, partly void

of it. In some few places the epithelium is so well preserved that even its ciliæ can be seen, in others it has become flattened, or has degenerated completely, so that detached cell remnants only are seen. Many of the cavities in the spongy layer contain such degenerating epithelial cells or hyaline balls or spheres, or both of these elements. In the deepest layer of the spongiosa these cavities, now already partly surrounded by muscular tissue, present the following appearance: They are not long-stretched clefts, but more or less round in outlines, their walls are folded toward the lumen, the epi-

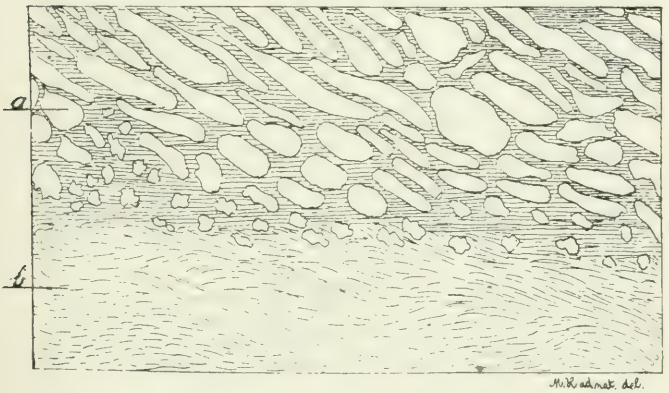


Fig 3. Spongiosa of serotina. (Leitz obj. No. 1, eye-piece No. 1.) a. Spongiosa with large gland spaces; b. Muscular coat of uterus.

thelial lining is well preserved. One beholds such a picture as is frequently seen in glandular hypertrophy of the uterine mucous membrane of a very marked type. The folding of the gland walls is due, in the case of the decidua, to the same cause that brings it about in the pathologic condition referred to. The gland wall—i. e., its basement membrane—and epithelium have grown more rapidly than the surrounding tissue, consequently foldings are formed toward the gland lumen.

The gland spaces are separated from each other by a tissue composed of decidual cells. Often the separating

tissue has become a mere narrow bridge or strip. The narrower these bridges the more the decidual cells are

Fig. 4. Decidua and intervillous space. (Leitz obj. No. 3; eye-piece No. 3.) a. Gland space, filled with mucoid material and hyaline spheres; b. Decidua serotina; c. Blood space in serotina (venous sinus); d. Maternal blood vessel (utero-placental vein) opening intervillous space; e. Intervillous space; f. Villus with blood vessel cut transversely and therefore appearing as an island unconnected with its villus; h. Hæmatoidin plates and needles; i. tortuous artery in decidua serotina cut transversely in three places

changed from their most characteristic type. They become smaller, more elongated, finally truly fusiform, so that they can hardly, if at all, be distinguished from

what they originally were—ordinary fusiform connective tissue cells.

The gland spaces of the decidua, I find, are more or less filled with cell remnants, and, as remarked before, with mucous or a homogenous hyaline material. They are certainly not filled with blood, as Gottschalk[8] *has stated.* This author has twice had a chance to examine a placenta *in situ,* obtained *per operationem* by Landau from the living. But in both cases the specimen was not handled in such a manner as to exclude hemorrhages into places where they might afterward be mistaken for normal conditions. In one case particularly, the uterine wall was perforated, the ovum torn open, the embryo decapitated and a hemorrhage produced into the amniotic cavity. Gottschalk must either have mistaken the true blood sinuses for gland spaces, or in his cases the blood, if indeed found freely in gland spaces, had gotten there in consequence of a traumatic hemorrhage.

In studying the utero-placental blood vessels in my specimen, I have found that the veins form large blood sinuses in the decidua, as has especially been pointed out by Waldeyer. The walls of these blood sinuses finally lose all their constituents, except the endothelial lining, and they run almost parallel to the surface of the decidua, and open as wide slits into the intervillous space. I have, however, not been able to trace any vessel with the characters of an artery into the intervillous space. While my specimens show in the decidua itself, somewhat distant from its surface, arteries with their characters as described by Waldeyer ("bindegewebsscheide," great tortuosity, etc.), I could not trace anything with the characters of an artery into the intervillous space. I think that the arteries, just like the veins, lose their walls so completely that they can not be recognized any more as arteries. Waldeyer made his studies on double injected specimens, where these things could,

of course, be more easily distinguished; in my specimen, for obvious reasons, no injection was made.

The specimen under discussion also shows how the endothelial cells of blood sinuses opening into the intervillous space are continued for a certain distance over the surface of the decidua. Yet I can not find that the whole surface of the serotina is lined by endothelial cells. One often finds on the serotina, even in places distant from the opening of a vessel, flat cells, but I consider them as remnants of the much-changed original epithelium lining the non-pregnant uterine cavity. I base this view upon the observation that such very flat cells I

Fig. 5. Decidua vera. (Leitz obj. No 7, eye-piece No. 3.) a. Flattened uterine epithelium; b. Typical decidual cells, some showing two nuclei.

found high up on the surface of the vera, where it had been strongly compressed upon by the growing ovum. In this situation those flat cells can neither be vascular endothelium nor changed syncytium; they must be changed uterine epithelium. As to the claim of Waldeyer and Keibel that the whole of the intervillous space is lined by vascular endothelium, I most certainly must dispute this, since my specimen does not show anything to confirm this assertion. There is certainly no endothelial lining over and above the syncytium of the chorion and the villi. The *decidua vera* may be very briefly described. It consists, like the serotina, of a compacta and a spongiosa. On the gland spaces the epithelium is generally more or less preserved. They are filled with mucus, etc., like the same spaces in the serotina, and oc-

casionally a gland duct still leads to the surface, but it is, however, as a rule, closed by the apposition of its walls. The vera is lined by a complete epithelial coat. High up, where the vera has been compressed upon very much by the ovum, this epithelium is, as remarked above, very flat; lower down it becomes cuboidal. Cylindrical cells or ciliæ are, however, not seen. The blood spaces of the vera are large, though not as large as those of the serotina. Of course, they do not open on the surface, but are closed. The gland spaces next to the muscular coat are like the analogous spaces in the serotina. The vera, like the serotina, shows patches of tissue in a process of coagulation necrosis.

The substance known as *canalized fibrin,* which, in the latter stages of pregnancy, is found in great abundance on the surface of the serotina, is already found, to some extent, especially near the margin of the placenta. Besides other stains employed for its study, Weigert's fibrin stain was used. While it did not prove fully satisfactory, it was of some service. It seems that the formation of the fibrin started in the decidua reflexa, extending from there to the margin of the placenta, and to its middle. It appears further, that the fibrin is first deposited between layers of degenerating decidual cells. The fibrin, I think, is derived mainly, if not entirely, from the blood of the intervillous space. There is no fibrin found on the vera, where we have no intervillous space.

The *decidua reflexa* in our specimen arises gradually out of the serotina by a gradual change of direction. The serotina as it approaches the margin of the placenta becomes thinner and thinner, the decidual cells become less characteristic, smaller and more closely packed, more fusiform with their long axis parallel to the long axis of the membrane; the leucocytes are increased in number. At the same time, chorion and decidua serotina approach each other more and more, and the inter-

villous space becomes gradually shallower. Finally, chorion and decidua reflexes touch each other. The latter consists almost entirely of a hyaline tissue which still shows some fine parallel wavy fibrillation. The greater the distance from the point where the decidua reflexa arises out of the decidua serotina—in other words, the more one approaches the antiplacental pole—the thinner and the more uniformly hyaline the reflexa becomes. Even, however, at the antiplacental pole, the substance of the reflexa shows blood spaces (sinuses) still containing the remnants of blood. These are evidently what is left of a once very vascular early decidua reflexa.

It has been mentioned before that the chorion at the antiplacental pole still bears small degenerating villi. These latter which are here attached to, or rather pressed against, the antiplacental part of the reflexa are surrounded by small blood spaces. These were once a part of the general intervillous space, now confined to the placental area, but once surrounding the whole of the chorion.

The *intervillous space*, which is bounded on one side by the chorion, on the other by the decidua serotina, and which contains the adherent as well as the floating villi, contains *maternal blood*. This fact to-day is conceded by every competent observer. The first one who clearly maintained that this was the case was E. H. Weber[9]. Since he made this assertion this view has been alternately confirmed and contested, until finally, in consequence of the investigations of Waldeyer, Langhaus, Nitabusch, Minot, Leopold and others, it has now been universally adopted.

In my sections the intervillous space is everywhere filled with blood, which, as was stated above, can be easily traced to the maternal blood sinuses.

The maternal blood, as found in the intervillous space, offers some very obvious points of differentiation from the fetal blood, as it can be studied in the blood vessels

of chorion and villi. The fetal blood is very much richer in nucleated corpuscles than the maternal blood. In fact, in the former, the proportion of the nucleated corpuscles to the non-nucleated erythrocytes is very much increased beyond what is found in adult normal blood, rising perhaps as high as 1:50 or even higher. The nucleated corpuscles are partly nucleated red ones, partly leucocytes. Nucleated red corpuscles do not seem to be very numerous, though I am not very positive about this, since the differentiation between a mononuclear white and a nucleated red cell is quite difficult, and, as it seems, uncertain.

Another point I have noticed in connection with the fetal blood in the placenta is the almost entire absence of polymorphonuclear leucocytes, almost all of the white corpuscles being of the small mononuclear type.

It also appears to me, judging from the effect of eosin stain in saturated glycerin solution, that the fetal red blood corpuscles are richer in hemoglobin than those of maternal origin, as found in the intervillous space. In the latter, the proportion of the white to the red blood-cells does not seem to show any great changes from the normal. The white corpuscles in the intervillous space are mostly of the polymorphonuclear variety.

The above observation may furnish another, though perhaps at this date, hardly needed proof, that the blood in the intervillous space is not the same blood as that in the fetal blood-vessels. Blood of maternal origin as found in the intervillous space is of quite a different type and composition from the blood of the embryo.

I now come, in conclusion, to another observation—as far as I am aware not made by any previous investigators, and not recorded in the literature upon the placenta. This observation seems to me to be of a good deal of physiologic as well as pathologic interest.

The intervillous spaces, normal and unaltered, by any post-mortem changes, as they must be from the manner

in which the specimen was obtained, and prepared, contain a very considerable number of *hematoidin plates and needles.*

The examinations for these derivatives of degenerating red blood corpuscles were made on stained and unstained sections, and on non-embedded pieces of tissue. The hematoidin presents itself in the form of rhombic plates and clusters of very fine needles. Often one sees a mass of hematoidin like a plate, but thicker and less regular, somewhat club-shaped on both ends and constricted and lighter in color in the middle. Such forms consist of a plate, both ends of which are thickly beset with fine needles. The picture reminds one of a straight magnet which has been dipped in iron filings, these having been attracted by and collected around the two poles. Thin plates of hematoidin are yellowish-brown in color, and so are the points of the needles which stand out around the darker center of the star-shaped clusters. All of these crystals give the typical hematoidin reaction with the sulphuric acid test.

The hydrochloric acid, ferro-cyanide of potash test for hemosiderin was negative; this iron-containing waste-product of degenerating red blood corpuscles was not found.

The hematoidin is, as stated, found all over the intervillous space; it is also found in the canalized fibrin, in the most superficial layers of the serotina, and also to a slight extent in the superficial maternal blood sinuses of the serotina, also in the small blood space between the chorion laeve and decidua reflexa.

Nowhere is this hematoidin found in fetal blood. The chorionic vessels and those of the villi are absolutely free from it. This fact is quite important, as it proves, aside from the nature of the specimen, that any idea as to a post-mortem nature of the hematoidin found can and must be discarded. Hematoidin is evidently formed in the maternal blood circulating very

slowly in the intervillous space, and found only there and in its immediate neighborhood.

It ought to be remarked that in order to carefully study the exact distribution of the hematoidin and not to be misled by a few crystals carried into a foreign territory by the cutting knife, the latter must be carried over the block first in one and then in another direction.

It appears that the finding of a derivative of decomposing blood in the intervillous space of an early placenta is of a good deal of interest. It seems to prove, in the first place, that this space is not simply a maternal blood space, is not, as has been claimed, lined by vascular endothelium. If it were, there is no reason why the blood should decompose in it even if the circulation is slow. As far as I am aware, blood circulating inside of a properly lined blood channel never decomposes to such an extent that a large amount of hematoidin is formed.

But the blood in the intervillous space is only partly enclosed by maternal tissue, and by no means contained throughout in vascular endothelium. Therefore, the blood has a tendency to change and to decompose. The presence of hematoidin also speaks strongly for the assumption that the canalized fibrin is likewise a derivative of the blood in the intervillous space.

The question arises, What becomes of all of the hematoidin formed during pregnancy? It will certainly not all be deposited where it is formed, because some of it was found in the maternal venous sinuses in the serotina. It therefore appears that some of this hematoidin, at least, is taken up by the blood current and carried through the utero-placental veins into the general maternal blood current. It is probable that the hematoidin so taken up will be carried throughout the right side of the heart to be deposited in the lungs. If this is the case, we ought to be able to find it there after death occurring during or after pregnancy. This task might be made somewhat difficult on account of the anthracosis

usually found in the lungs of adults. Of animals which could be used experimentally to investigate this point, I think the only available ones would be those primates of which it is known that their placentæ are like the human one. Rodents could not be used, since their placentæ are of quite a different type. It would hardly be proper to theorize whether or not some of the subjective symptoms of pregnancy might be dependent upon the presence of hematoidin circulating in the maternal blood. But it seems reasonable to consider as very probable, a causal relation between the presence of hematoidin in the circulation of pregnant women and the peculiar marked frequency of embolism and thrombosis during gestation, and post-partum. In giving a short review of the above report, facts either not observed previously by other investigators of the subject, or facts noted previously but not confirmed, or details in which I differ from other well-known writers upon the placenta may now here be briefly recapitulated:

1. In the amnion, near the insertion of the cord, there were found small cavities contained between two layers of amniotic mesoderm. It is possible that these small cavities are due to a reduplication of the amnion occurring at a very early stage of its foundation.

2. The chorionic epithelium, and that of the villi, presents itself in two very distinct layers, each of characteristic differentiating features. The Langhaus "Zellschicht," has been found in a single cell layer only, nowhere as a double or a triple layer. The epithelium does not possess a basement membrane.

3. Plasmodial (syncytial) buds springing from chorion and villi are very abundantly found. Plasmodial islands in the intervillous spaces do not exist; what appears as such are buds separated from their bases by the direction of the cut of the knife.

4. Kastchenko's "Zellknoten" are likewise not at all islands floating in the intervillous space, but decidual

and syncytial tissue detached from the decidua in the same manner as the buds are detached.

5. The chorion at the antiplacental pole still shows remnants of villi.

6. The decidua serotina, as well as the vera, show already patches of tissue in a state of coagulation necrosis. Where this latter is manifest, there are found numerous leucocytes, many of which are in a process of nuclear fragmentation.

7. The decidua reflexa is in that stage of degeneration, as has been first minutely described by Minot. (l. c.).

8. Evidences are still found in connection with the decidua reflexa, which prove that it once was very vascular and that the intervillous space filled with blood once surrounded the whole ovum.

9. The decidua serotina is not throughout its whole extent lined by vascular endothelium, nor have chorion and villi such a lining.

10. Changed remnants of the original uterine epithelium are occasionally found on the surface of the serotina and everywhere on the surface of the vera.

11. The open spaces of the spongiosa, the changed uterine glands show epithelium varying from the normal to a stage of complete degeneration, and these spaces are not filled with blood, but with mucoid or hyaline material, cell remnants and hyaline spheres.

12. The intervillous space contains maternal blood which in its corpuscular elements is very different from the fetal blood found in the blood-vessels of the chorion and villi.

13. The main, if not the exclusive source of the canalized fibrin, is the maternal blood in the intervillous space.

14. In this space are also found numerous hematoidin crystals; these insoluble derivatives of degenerating red blood corpuscles are in part carried into the

utero-placental veins, and from there into the general maternal circulation. They stand most probably in a causal relation to the comparative frequency of embolism and thrombosis during pregnancy and post-partum.

Having been engaged for some time in the study of the early placenta and having examined placentæ and ova from two weeks to several months' old, I have above occasionally, though rarely, referred to conditions found at different stages. In order to avoid any misunderstanding, I want to emphasize that the observations recorded refer to the one placenta only. The favorable circumstances under which it was obtained seemed to warrant its separate description, which I hope I will soon be able to follow up by a comprehensive paper on the histology and development of the early placenta.

December 13, 1897.

BIBLIOGRAPHY

1 Minot: Uterus and embryo. Jour. of Morph., Vol. ii, p. 341; also Human Embryology, New York, 1897.

2 Waldeyer: Bemerk. ueb. d. Bau. der Menschen. u. Affen-Placenta. Arch. f. Microsc. Anat. Vol. xxxv, 1890.

3 Webster: Ectopic Pregnancy. Edinb. and London, 1895.

4 Leopold's great Atlas upon the placenta which has just now been published in Germany has not yet been accessible to me.—M.H.

5 Schaefer: Quain's Anatomy, Vol. i, Part i, p. 43.

6 Under the term epithelium of the chorion and villi I comprise collectively both layers, the "Langhaus Zellschicht," as well as the syncytium, holding with Minot, Graf Spree, Kastchenko, Hofmeier, Webster and others that they are both derived from the fœtal ectoderm.

7 Eden: A Study of the Human Placenta. Jour. Pathol. and Bacteriol., 1894-96, Vol. iii, pp. 449-471.

8 Gottschalk: Weitere Studien ueber die Entstehung der mensch. Placenta Arch. f. Gyn., Vol. xl, 1891, p. 169.

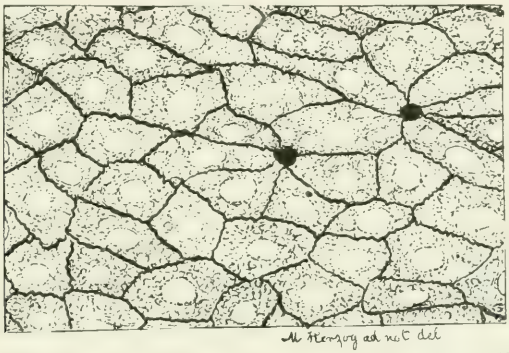
9 Weber: Hildebrandt's Handb. f. Anat. des Menschen iv. auft. Vol. iv, p. 490.

LYMPH-STOMATA IN THE AMNION.

MAXIMILIAN HERZOG.

The microscopic specimens exhibited come from a full term amnion which presented the unusual feature of being completely unattached to the chorion and separated

from it by a quantity of chorionic (not amnionic) fluid. This is a condition which is not frequently found in man, while it is the normal state of things in many of the mammals, for instance the sheep. I received this amnion and the other placental structures at once after they had been delivered together with a healthy, normal child. In order to immediately decide the question whether this amnion was covered on both sides with epithelium, it was silvered in the manner used ordinarily for the purpose of demonstrating intercellular cement substance, lymph-stomata, etc.



Amnion, full term. Silvered Leitz obj. No. 7, Eye piece No. 3.

It was found that the amnion was covered with epithelium on one side only; the process of silvering, however, demonstrated some interesting features. While with the ordinary methods the amniotic epithelial cells appear more or less as regular columnar cells, the silvering clearly shows that they are very irregularly polygonal. The cell boundaries are fine and irregularly wavy lines. The silvering shows very beautifully the vacuolation of the cell protopasm which has been demonstrated before with the ordinary staining methods. The silvering also shows that intercellular protoplasmic bridges, as has been claimed to be demonstrated do not exist. The most interesting feature shown is the following: Here and there one can see very dark spots, around which the epi-

thelial cells are grouped. The picture seen is identical with that of the lymph-stomata of the peritoneum and mesentery. It appears therefore that the amnion is a true serous membrane with lymph-channels and lymph-stomata.

Dec. 13, 1897.

M. L. HARRIS AND MAXIMILIAN HERZOG presented a report of cases of lipoma of the renal capsule June 14, 1897.

EMIL RIES read a paper upon "Tumors of the Wolffian Body and Duct," December 13, 1897.

CARL WAGNER reported a case where a large sarcoma of the ovary complicated pregnancy, February 14, 1898.

MARIE J. MERGLER demonstrated specimens; 1, a rapidly growing fibromyoma of the uterus; 2, a fibromyoma of the round ligament, March 14, 1898.

J. L. MCCOLLUM presented a specimen showing very marked tumor metastasis in the omentum from an adeno-carcinoma of the ovary, May 9, 1898.

THE LYMPHATIC SYSTEM.

HODGKIN'S DISEASE.

GREAT DECREASE IN SIZE OF TUMOR MASSES UNDER INTERCURRENT ERYSIPELAS; RAPID RECURRENCE; DEATH. UNUSUALLY EXTENSIVE LYMPHOID INVOLVEMENT OF ALIMENTARY TRACT SHOWN POST-MORTEM.

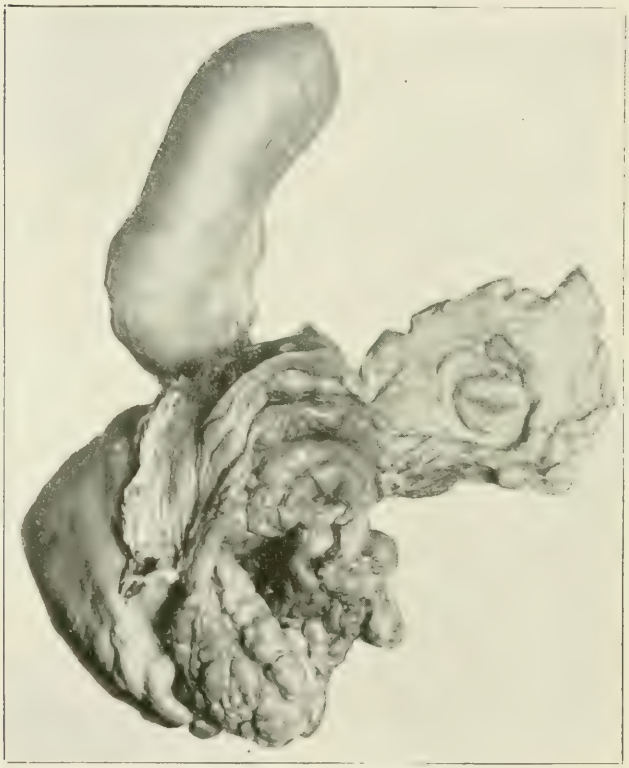
JAMES B. HERRICK.

J. C., Bohemian, about 45, noticed enlargement of glands on right side of neck three months before entering Cook County Hospital. During these three months other glands in the neck, axillæ and groins had become painlessly enlarged. But slight effect on general health; few pressure symptoms though mediastinal glands and abdominal glands were on physical examination, enlarged. No leukæmic blood changes. Whole appearance typical of rather acute Hodgkin's disease. No improvement under arsenic.

In about two months erysipelas accidentally developed in the right arm, and extended in migratory fashion over head and chest, the whole attack lasting fully two weeks. Several subcutaneous phlegmons were opened from which the streptococcus pyogenes alone was recovered. Patient at one time so extremely ill with high temperature, rapid pulse, emaciation, weakness, delirium that recovery regarded as doubtful. Gradual improvement and disappearance of erysipelatous symptoms.

During this attack the glandular masses diminished

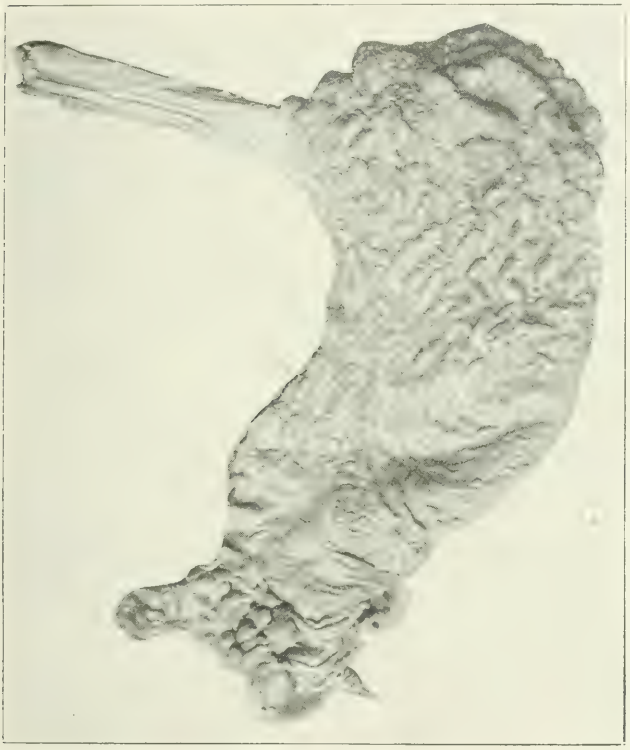
in size rapidly and in a most remarkable manner. Tumors in the neck, groins and axillæ decreased from the size of the closed fist to that of an olive or hazel-nut. The change in the man's appearance was most striking, especially as the emaciation was marked.



Veriform appendix unopened: cecum and ilium opened.

Though erysipelas toxins were later used there was a progressive increase in size of the tumors. All the palpable glands became greatly enlarged, there were physical signs of mediastinal growths. Evidence of obstruction to respiration and swallowing became more pronounced, anemia increased, there was some edema

and great loss of flesh, and the patient died from general asthenia in a year from the beginning of his symptoms.



Stomach opened.

The autopsy (Dr. Hektoen) revealed enormous tumor masses in the neck and mediastinum making pressure on the esophagus and trachea (specimen presented). The nares and pharynx were filled with nodules; the tonsils met in the center. There was free fluid in the pleura. The lungs were unevenly infiltrated with tumor masses. The heart, kidney, liver contained no nodules; the spleen held one. Large tumors were in either groin.

The intestines, large and small, showed general enlargement of the lymphoid nodules; Peyer's patches and the solitary follicles were all markedly increased in size. On the external surface these enlarged areas showed black. The cecum was filled with hard, blackish nodules and masses attached to the wall of the intestine. The appendix vermiformis was greatly enlarged, being thicker than a man's thumb. Its lumen was filled with hard nodular masses and its opening into the cecum occluded.

The esophagus contained many enlarged nodes. The mucous membrane of the stomach was rough and uneven and filled with small nodules, even up to the size of a hazel-nut. Some nodules here, as in the intestine, were polypoid in appearance.

The points of especial interest in the case are:

1. The marked decrease in the size of the tumors under the influence of a migrating erysipelas.

2. The prompt renewal of the growth of the tumors as the erysipelas disappeared.

3. The universal enlargement of the lymphoid structures in the alimentary tract, tongue, pharynx, esophagus, stomach, small and large intestine.

March 8, 1898.

THE MORBID ANATOMIC EVIDENCES OF THE LYMPHATIC CONSTITUTION IN IDIOPATHIC EPILEPSY.

A. P. OHLMACHER.

In the course of an investigation into the pathology of epilepsy, carried on since last July at the Ohio Hospital for Epileptics, a series of uniform and hitherto undescribed conditions have been found at autopsy in certain cases of epilepsy, and it is to these particular

conditions that your attention is respectfully invited.

It is scarcely necessary to remind you that no constant gross or microscopic lesion has been discovered in epilepsy, especially in what we might style "pure" epilepsy, or "primary" epilepsy, or idiopathic *grand mal.* This may, in part at least, be due to the fact that attention has too exclusively been concentrated upon the central nervous system to the neglect of the body as a whole, and that too much weight has been laid upon changes in the brain which are doubtless of a secondary character, due to the action of some extrinsic cause. This poverty as regards somatic details will be fully appreciated by anyone who searches the literature of epilepsy with the desire of obtaining post-mortem records in which the data has been determined with that exactness and fulnes sdemanded by modern pathologic research.

It was precisely this condition of affairs that led us, on commencing our work, to look with especial care to the gross and microscopic pathology of the cases which came to autopsy, in the hope that the data carefully gathered and reliably recorded would ultimately furnish statistics from which conclusions could be drawn; and that eventually there might be established what has always been lacking as a foundation for the study of epilepsy, and what is fundamental for the rational study of any disease, viz., a morbid anatomy.

Eighteen cases have been examined post-mortem since this work was inaugurated, and in eight of these cases some distinctive features were met, which, from their comparative constancy and singularity were regarded as more than accidental occurrences. These eighteen cases represented various types of epilepsy and the insanities accompanied by epileptoid phenomena. The findings at autopsy naturally varied widely in these cases, as would be expected from their clinical diversity. The details with reference to the first six of them were recorded in the *Bulletin* issued by the hospital last January; and in

another publication, to be ready in a short time, the full account of the eighteen cases will be given.

So far as the clinical side is concerned it is important to note that these eight cases include all of the examples of typic idiopathic *grand mal* which have thus far been examined at post-mortem. The patients were all young adults, varying in age from 17 to 35 years. All of them, except one, suffered with epilepsy from childhood. Four of them had periodic epileptic mania. One man died from maniacal exhaustion: one committed suicide: two women and one man were found dead in bed after having retired in apparent good health, which is to say (and this should be emphasized), that out of the eight cases there were three instances of sudden death, in at least two of which no lesion to account for the abrupt ending could be found.

The gross pathologic anomalies in these eight cases, which are illustrated by the specimens to be submitted for your examination, may be summarized as follows: A persistent, enlarged, and apparently active thymus body; a pronounced hyperplasia of the intestinal and splenic lymph-follicles; a more or less marked hypertrophy of the lymphatic glands, and of the lymph-adenoid follicles of the tongue, larynx, trachea, esophagus, tonsils, and even of the stomach; a narrowing of the arteries; an abundant development of fat; an enlargement of the thyroid; and certain osseous changes indicative of old rickets. Not all of these abnormalities were present in a single case, though the persistent thymus, with one or more features added, was constant. With the specimens before you it will not be necessary to enter into minutiæ of description since you will readily recognize the thymic body, the enlarged follicles, narrow arteries, etc.

Taken collectively, these morbid anatomic conditions make a picture of what the German pathologists style the "lymphatic constitution." The evidences of the

lymphatic constitution have been noted for a number of years in connection with several diseases, but never, so far as I can determine, have they been described in connection with epilepsy.

There are two morbid conditions, accompanied by a more or less perfect picture of the lymphatic constitution, which seem especially important in relation to what we have found in our epileptics. One of them is laryngismus stridulus, or more exactly, what the Germans style "thymic asthma," which is well known clinically, and which is often responsible for very sudden death in the infants affected. The other condition is sudden death in apparently healthy adults with no assignable lesion, and in whom only the persistent thymus, with other evidences of the lymphatic constitution, is found at autopsy. It is impossible to discuss these extremely interesting morbid states in the time at our disposal, and it must be sufficient simply to emphasize the fact that the morbid anatomy of the lymphatic constitution is peculiar, not only to these conditions, but, apparently also, to at least certain cases of idiopathic epilepsy. Of this morphologic analogy there can be little doubt, and in the report upon four of our cases in the January *Bulletin*, arguments were advanced for defining a clinical as well as anatomic analogy between thymic asthma, thymic sudden death, and epilepsy.

What the significance of the lymphatic constitution is, in its relation to thymic sudden death, is not at all clear, although numerous hypotheses have been called into account: and this is precisely the case in relation to our own work where this peculiar anatomic picture has been shown to occur in certain epileptics. Without resorting to pure speculation the present state of our knowledge in relation to the lymphatic constitution prohibits an explanation, and since speculation has played too exclusive a part in the attempts to account for that myster-

ious malady, epilepsy, we propose to refrain from indulging in this very tempting pastime.

With this naturally very much condensed introduction, which will, I trust, make them more intelligible, I beg to submit the specimens which illustrate the persistent and hyperplastic thymus; the intestinal and splenic lymphatic hyperplasia; the narrow arteries; the hypertrophied lymphatic glands; and the excessive development of fat; which were obtained from three of the eight epileptics, all of whom presented the typic picture of the lymphatic constitution at autopsy.

May 9, 1898.

LYMPHOSARCOMA OF THE MESENTERY.

MAXIMILIAN HERZOG.

Some time ago Dr. M. L. Harris[1] and myself reported a case of lymphosarcoma of the mesentery operated on successfully in a boy of 5 years old. When I then collected the literature of the subject, I was able to tabulate a total of 57 cases of solid mesenteric tumors, of which about 10 were sarcomata. To the latter class I am now able to add a new case. As in most instances of solid mesenteric tumors, the exact diagnosis as to location was not made *intra vitam*. For a short abstract of the history of the case, I am indebted to Dr. R. B. Preble, under whose care the patient was during his last weeks of life. The history is as follows:

Sept. 14, 1898, H. G., German, 62 years old, physician. He traveled extensively as a young man, living for a time in Asia, where he escaped all diseases except a mild malaria; has lived many years in Chicago. About six years ago he discovered a moderate glycosuria, which disappeared on a course of Carlsbad treatment. The glycosuria never, to his knowledge, returned. He had been a moderate drinker all his life; never had syphilis. The present illness is of rather indefinite onset, both as to time and symptoms, but he must have been ailing

for about two months. He has continued to do his medical work up to one week ago, and complains only of weakness, dyspnea, moderate constipation, and of the increasing size of the abdomen. A short time ago he had what he describes as an epididymitis[2] followed by swelling of the lymph glands below Poupart's ligament. It continued only a short time, and has now entirely disappeared. He has had no vomiting, no diarrhea, no jaundice, no hemorrhages.

Examination.—Well nourished and rather fat man, apparently about 60 years old; no jaundice, no cyanosis; moderate dyspnea, moderate edema of the feet. Lungs: lower borders high, but move freely on respiration; no râles, no fluid in pleural cavities. Heart: displaced upward by the digh diaphragm, but normal in size. Tones pure and of normal intensity. Pulse: regular, strong, normal. Abdomen: prominent, contains large amount of free fluid, which changes promptly with change of position. No varicose veins. Liver: can not be palpated, nor outlined by percussion. Spleen: palpable. Lymphatic glands: below Poupart's ligament both sides about the size of a hen's egg; elsewhere not palpable. Urine: contains no sugar, albumin nor casts. Blood examination, negative.

Diagnosis.—Atrophic cirrhosis of the liver, based on ascites, palpable spleen, absence of any other manifest cause for ascites and the history. The enlarged glands in the groins are not accounted for except as the probable result of an ulcer of the leg.

Treatment.—Diuretics, salines and mild diet.

The fluid in the abdomen gradually increased, causing dyspnea, until it was decided to tap the patient. Withdrew 6000 c.c. of milky fluid, s.g. 1012, large amount of albumin, sugar, 2 per cent. The fluid cleared on being shaken with ether; contained few round mononuclear cells with fat granules. The fluid was that of a chylous and not of an adipose ascites. After withdrawal of the fluid, large numbers of tumor masses could be felt throughout the abdomen. After the tapping, the patient rapidly lost strength, developed an edema of the dependent portions of the body, and on the last day a very slight icterus.

Clinical diagnosis.—Tumor abdominis, probably carcinoma, but there is no evidence pointing to the primary organ. Chylous ascites due to obstruction of thoracic duct by the tumor.

The post-mortem was made by the author, Oct. 16, 1898—fifteen hours after death. The protocol of the autopsy reads as follows:

The body is that of a very strong, heavy man, about 60 years of age; estimated weight 250 to 260 pounds; well nourished. Post-mortem rigidity and lividity well

marked; extensive edema of the lower extremities, more marked on the right than on the left side; edema of the scrotum. The skin of the legs is hard and brownish in color. Between the umbilicus and the symphysis pubis, to the left of the linea alba, is a circular trocar wound, almost closed. On making the primary long incision the whole skin over thorax and abdomen is found to be edematous, a clear fluid oozing out from it.

The abdominal cavity contains from two to three gallons of a yellowish, very turbid ascitic fluid. The right pleural cavity contains quite a large amount of clear fluid; the exact amount can not be estimated, since on manipulation ascitic fluid from the abdomen runs over into the pleural cavity and mixes with the clear pleuritic transudate. The pericardium is smooth and contains in its cavity a slightly increased amount of pericardial fluid. The external surface of the heart—which latter is of normal size—shows a moderate amount of fat; the myocardium is soft, flabby and pale; the orifices are normal in size; the endocardium is smooth over its whole extent; the valves are normal. The intima of the large vessels is smooth; the walls of the coronary arteries are somewhat stiff and thickened, their intima, however, is perfectly smooth.

Lungs: No adhesions on either side; quite an amount of clear fluid on the right side. The lower lobe of the right lung shows, on its anterior surface, several subpleuritic, flat, grayish-white patches, raised slightly above the surface; there were also found in the pulmonary parenchyma several firm, hard nodules, likewise of a grayish-white color. The entire lower lobe of the right lung, on section, appears more or less collapsed and solid; pieces from this part, however, still float on water. The lower lobe of the left lung also contains several hard nodules of the same type as those mentioned above. Both lungs are markedly edematous throughout. On the left pleura

costalis, about the region of the fifth rib, in the axillary line, are found some small grayish-white, slightly prominent patches. The bronchial glands on either side are enlarged, firm and nodular, and on section, appear grayish-white and somewhat translucent. In the glands, from which small amounts of whitish material may be scraped, are numerous hemorrhagic spots. The omentum majus is studded throughout its whole extent with firm, grayish-white nodules from a few millimeters to one centimeter in diameter.

The spleen is large, smooth, quite firm and dark—brownish-red on section; the trabeculæ stand out distinctly and prominently. The kidneys are of normal size, capsules smooth, easily detachable; cortex and medulla normal in size and proportion; cortical markings fairly distinct. The mucous membrane of the pelvis is smooth. The adrenals, more or less embedded in tumor masses, show very marked pigmentation on section; their substance, however, is uniformly soft. The mesentery, the head of the pancreas, the retroperitoneal glands and the omentum minus form one large, irregular tumor, the component parts of which are united to each other more or less firmly by nodular masses. The mesentery and the retroperitoneal glands form a tumor mass as big as two large fists; the omentum minus is irregularly infiltrated with firm nodules; the head of the pancreas presents a roundish mass four or five centimeters in diameter. In the rest of the pancreas, the glandular tissue appears normal, with the exception of some small hemorrhagic foci. To the tumor involving mesentery and head of the pancreas, part of the circumference of the duodenum is firmly attached. The lumen of this gut, however, does not show any marked constriction, and there is no impediment to the flow of the bile, which, on slight pressure upon the gall-bladder, escapes through the common duct. The stomach appears normal. On the

under surface of the head of the gall-bladder there are three flat, grayish-white, somewhat prominent subperitoneal patches. The gall-bladder contains thickened, cloudy, dark-green viscid bile. Its mucous membrane is smooth.

The liver is small in size, nodular and uneven over its entire surface. The liver tissue is firm and uneven on section. Masses from the size of a pin-head to that of a millet-seed rise above the level of the cut surface and make it uneven. Several small nodular, grayish-white, enlarged lymph-glands are found behind and around the thoracic aorta directly above the diaphragm. The lymphatic vessels can be followed downward behind the peritoneum, as several parallel white bands extending far down into the pelvis. The left inguinal glands are hard and firm, enlarged to the size of a large walnut, and on section, are found to be studded with grayish-white translucent nodules.

Anatomic diagnosis.—Malignant neoplasm of the mesentery and retroperitoneal glands; metastases in the head of the pancreas, the omentum minus and majus, the lymphatic glands on the neck of the gall-bladder, the pleura costalis and pulmonalis, the bronchial glands on either side of the lymphatics along the thoracic and abdominal aorta, and the left inguinal glands. Compression atelectasis of the lower lobe of the right lung. Chronic passive congestion of the spleen. Cirrhosis of the liver. General anasarca.

Microscopic examination.—The tumor masses in the mesentery, in the omentum, in the head of the pancreas, in the inguinal glands, and in the lungs, are all of the same structure. They consist of small, round cells of the type of the ordinary small lymphoid cell. The nucleus is quite rich in finely glanular chromation, the cell protoplasm very scanty. Besides those cells there are found in other areas round cells, slightly larger than the former; they are more of the

type of those cells found in the proliferating center of Flemming in the lymph follicle. Their nuclei are larger, and the chromatin is not as finely, but more coarsely granular; the cell protoplasm is not quite as scanty. The tumor cells are contained in a meshwork or matrix of fine connective tissue fusiform cells and fibers. These cells and fibers are not very abundant, still they are much better developed than they are in the normal lymph follicle. The blood-vessels in the tumor masses are moderately numerous and not very large. In places, free blood is found between the tumor cells. Large areas of the neoplastic tissue show necrobiotic changes. All cells in such territories have lost their nuclei, and the cell body has become somewhat swollen and indistinct in outline; the degeneration has, however, nowhere progressed to the formation of hyalin or colloid material. This is noted expressly, since in the other case of lymphosarcoma of the mesentery reported by Dr. M. L. Harris and myself[3] there was very extensive colloid degeneration.

The above microscopic description refers more or less to all the tumor masses. However, it ought to be stated that the most marked and most extensive regressive changes are present in the large tumor mass, found in and developed from the mesentery. Here we see great tracts of necrobiotic tissue and also areas of fatty degeneration. The areolar tissue itself presents fatty changes; its meshwork is very poor in nuclei and shows a great deal of fine vacuolation. The necrobiotic areas, in a finely granular mass, show comparatively few nuclei with hyperchromatosis, nuclear fragmentation, karyolysis and free chromatin granules. The tumor mass most distant from the mesenteric tumor, namely, the one in the inguinal glands, on the other hand, shows very few regressive changes, but presents clear and distinct cells and like nuclei, some with karyokinetic figures. Evidences of fat necrosis were not found.

The body of the pancreas is fairly normal, so far as the parenchymatous glandular tissue is concerned; the interstitial connective tissue, especially that around the small ducts, is increased in amount.

In the liver there is seen a proliferation of the intra-acinous periportal connective tissue; there is, however, no proliferation of the intra-acinous connective tissue. The proliferative processes are evidently active and progressive, since the intra-acinous tissue shows numerous newly formed blood-vessels and a proliferation of the bile-ducts. The tissue between the lobules also shows a very abundant infiltration, with small, round cells, all of the type of small lymphoid cells. Polymorphonuclear leucocytes were not found in the intra-acinous septa. The liver-cells proper are normal in size and arrangement. There is very little fatty degeneration in the lobules. Many of the intralobular bile capillaries, especially those near the periphery of the lobule, are much distended and filled with bile pigment. The liver-cells in the immediate neighborhood of such distended bile capillaries contain a considerable amount of granular bile pigment.

Epicrisis.—The mesentery, in which was found by far the largest tumor mass, was undoubtedly the primary seat of the lymphosarcoma, which subsequently gave rise to metastases in the pancreas, omentum, lungs, a number of lymphatic glands, etc.

The ascites, as such, was due to the cirrhosis of the liver. Its peculiar nature, i. e., that of a chylous ascites, must be explained by pressure on, and perhaps, complete obstruction of, the thoracic duct, by lymph-glands enlarged and hardened by tumor metastases. The sugar found in the peritoneal fluid may be looked upon as a vicarious excretion of a pathologic metabolic product due to the extensive pancreatic involvement.

It is by no means obvious that the advanced cirrhosis of the liver in the present case was due entirely or even

partly to alcohol. The deceased had certainly during the last six years of his life, i. e., after his transitory diabetic attack, been a very moderate drinker only, and he had never had any symptoms of cirrhosis except during the last weeks of his life. It does not appear entirely unreasonable to assume that the advanced cirrhosis of the liver, giving rise to definite symptoms only toward the latter part of a comparatively short illness, may have been due to toxins derived from the large and widely spread sarcomatous masses in the abdominal cavity and brought to the liver by the portal circulation.

This possibility, I think, can not be viewed as an absurdity, but rather deserves some consideration, if we look upon it in the light of the contributions upon the subject of cirrhosis of the liver by Adami[4] and by Hektoen and Weaver, who quite recently reported to this society observations on cirrhosis of the liver in the guinea-pig, due to bacterial infection and to the circulation of toxins in the liver.

January 10, 1899.

LYMPHOMA: A BENIGN TUMOR REPRESENTING A LYMPH-GLAND IN STRUCTURE.

E. R. LE COUNT.

I am indebted to Dr. J. B. Murphy for the opportunity to examine a small tumor, which from a careful study, I became convinced represents a benign non-inflammatory, new growth of lymph nodes; in other words, a lymphoma, according to Senn, a benign lymphoma according to Zeigler and others. The tumor was located in the left groin and it had reached the size of a pigeon's egg by a very gradual growth for a number of years. The left inguinal canal was closed; there

was no enlargement of the adjoining lymph glands nor were the lymph glands of the opposite side enlarged. The man was in good general health. He had been in good health for a number of years; there were no similar tumors elsewhere on the body and since the removal of this tumor three years ago there has been no recurrence.

FIG. 1. The tumor exact size cut in halves and laid open. From the right half a segment has been removed.

Examined in the fresh condition it was oval and flattened and not very unlike a small kidney in shape. On cutting it light reddish surfaces were exposed which were besprinkled with small millet-seed-sized and somewhat smaller light areas. These areas resembled greatly the Malphigian bodies of the spleen; they were found to be uniformly distributed over the cut surfaces and in this regard there was no difference between the subcapsular regions and parts more centrally located. A fibrous capsule surrounded the growth, but no coarse trabeculæ entered its substance. Further, the growth showed no points of hemorrhage or softening; the blood-vessels exposed were all small.

Microscopic examination shows the tissue to be dis-

tinctly lymphoid in structure and made up very largely of lymph nodes. The cells composing these nodes are arranged in a very peculiar fashion. Around the periphery they form rows which extend for one third and in rare instances one-half of the distance around the circumference. The arrangement in rows is more perfect in some nodes, but in serial sections it is found present to some degree in every node. Frequently the rows are double or three or four rows form a band which ex-

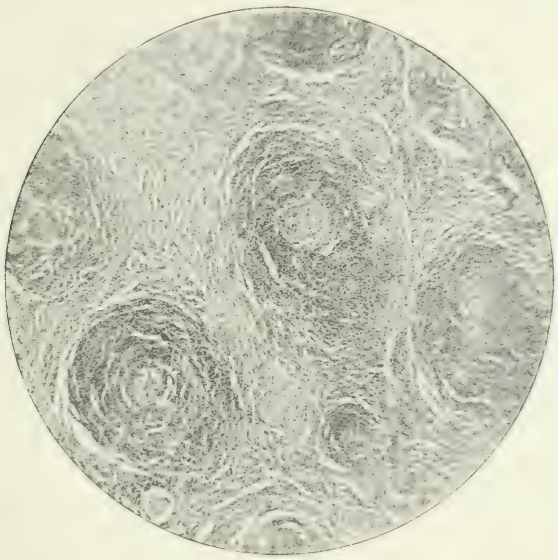


FIG. 2. Lymph-nodes.

tends around a node for some distance and breaks up to anastomose with similar bands or single rows. Between the rows and bands are cleft-like spaces due to unequal shrinkage in the alcohol with which the tissue was hardened. The edges of the nodes are distinct, as a rule, but in some nodes the rows at the edges jut out into the surrounding tissue. The cells forming these rows are 4 to 5 mikrons in diameter with a nucleus occupying almost the entire cell, only a narrow margin of

body protoplasm surrounding the nucleus. The nuclei are round with a deeply staining nuclear membrane. The chromatin frequently forms an irregular lining for the nuclear membrane and usually two or three centrally located large granules. The reticulum supporting these cells is very scanty in the outer zones; here

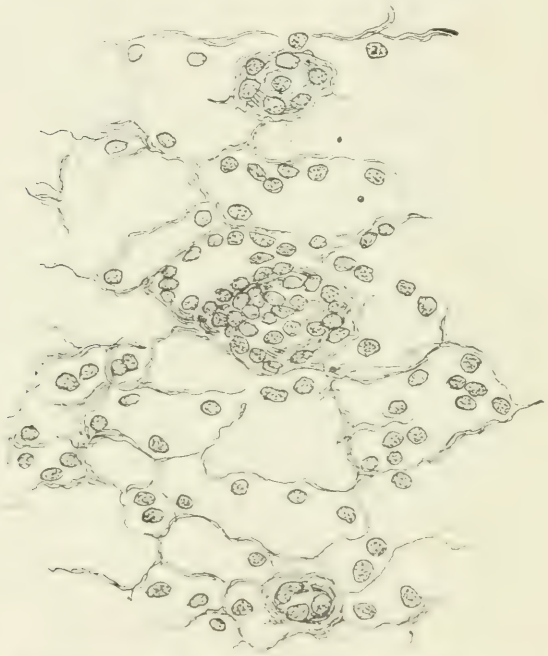


FIG. 3. Reticulum from a pencilled section stained with Van Gieson's stain.

it forms delicate strands which extend parallel and between the rows. Toward the center it is more dense and forms heavier bands. It is also more dense around the blood-vessels.

Blood-vessels are present in every node, usually two or three enter. Entrance is obliquely and division frequently takes place after entrance. In such instances the further course of the vessel is not easily made out.

These vessels are arterioles; their walls are thick and rather hyaline. In case the vessel is cut directly across the row formation is seen to be very perfect, row after row surround the vessel throughout the entire node. Each node also possesses a group of cells which affords a marked contrast to the cells which are arranged in rows. These cells are found in the center of the node or near it; they are large (8 to 10 mikrons in their long diameter); they possess oblong, irregular or notched, pale-staining nuclei. These cells occur at or near where the arteriole breaks up to form capillaries.

The internodal tissue is loosely constructed. It has considerable stroma which supports small cells similar to the darkly-staining cells of the nodes. They are most numerous at the edges of the spaces formed by the reticulum. The reticulum was studied by Van Giesen's staining method, in section stained by picro-nigrosin and by the iron-hematoxylin method. No nuclei could be found which could be positively affirmed to be a part of the stroma, not even in carefully pencilled sections. Larger blood-vessels occur in the internodal tissue. They possess two, three or even more, elastic sheaths. The thickening of arterioles and arteries has only affected their middle coat. The veins show no changes. Only in the large vessels is any trace of blood found. The external capsule is thin, largely fibrous with relatively few nuclei.

In conclusion the light areas found when the tumor was cut and which resembled the corpuscles of the spleen are found to be remarkably large lymph nodes formed largely by rows of cells which are extraordinary for their extreme regularity. These lymph nodes are arranged about blood-vessels and are in all respects similar to the lymph nodes described by His, Flemming and others and called by them the "secondary nodules" of lymphoid tissue.

February 14, 1898.

SPLENIC PSEUDOLEUKEMIA (SPLENIC ANEMIA—SPLENOMEGALIE PRIMITIV) WITH THE REPORT OF A CASE.

BERTRAM W. SIPPY.

The object of this article briefly stated is: 1, to further the recognition of a very rare and fatal disease to which the term splenic pseudoleukemia seems most applicable; 2, to contribute to its symptomatology and pathology; 3, to record the results of experimental research, employed with a view of determining its nature and etiology; 4, to present reasons why, in the light of our present knowledge and experience, the removal of the spleen is the treatment to be advised when the diagnosis is certain and the conditions not especially unfavorable.

HISTORY.

The history of splenic pseudoleukemia is inseparably connected with that of the diseases to which it is closely allied, namely: leukemia and the other forms of pseudoleukemia. Its study, therefore, may well trace the development of our knowledge of those diseases as a class.

The attention of the medical profession was early directed to a complexus of symptoms, characterized by enlargement of the spleen, pallor, hemorrhages, œdema and grave cachexia. Hippocrates wrote on the association of splenic tumor with dysentery, hemorrhage, scorbutus and miasmatic diseases. Galen described hypertrophy of the spleen in protracted autumnal fever and other cachetic states. Malpighi, Morgagni and others observed splenic and lymphatic enlargement associated with pallor, hemorrhage and emaciation, which progressed to a fatal tremination. Nivet (Archives Generales de Medicine, 1838) mentions scorbutus, rachitis and scrofula among the many causes of splenic en-

largement. In some of the cases of splenic hypertrophy reported by him under the heading of rachitis and scrofula, extensive glandular enlargement and grave cachexia developed during the course of the disorders. There is much in the literature of the older writers to indicate that they were quite familiar with hypertrophy of the spleen in miasmatic disease and that they also had noted the condition in various other affections such as scrofula, continued fevers, syphilis and liver disease. Now and then one also finds record of cases in which, without apparent cause, the spleen enlarged, hemorrhages and cachexia supervened and death followed.

No particular types of disease of this nature were well recognized, however, until in 1832, Hodgkin wrote his now well-known article on "Some Morbid Appearances of the Absorbent Glands and Spleen (Medico-Chirurg. Transactions). He reported a number of cases which showed an increase in the size of the lymph glands and spleen followed by emaciation, ascites, pallor, edema and death. The blood was not examined in any of the cases and the report, in many instances, is meager. One is able to discern, however, that undoubtedly the author's cases included carcinoma, tuberculosis, sepsis and probably other morbid conditions. Nevertheless, it was the first worthy attempt to group this class of affections.

In October, 1845, Bennet published his report of a case of hypertrophy of the spleen in which the blood of the patient contained a great number of white corpuscles resembling pus cells.

In November of the same year Virchow reported a similar case and correctly attributed the large increase in the white cells to an augmentation of the white blood corpuscles. He believed that the great increase in the leucocytes was due to the hypertrophy of the spleen. Subsequently, he evolved the doctrine of the disease, leukemia, which he described as an affection character-

ized by cachexia, enlargement of the spleen and lymph glands and an augmentation in the number of white blood corpuscles. Other histological changes in the disease described by him were cellular hyperplasia of the lymph glands and spleen and infiltration of lymph cells in the tissue of the liver, lungs, kidneys and intestinal tract. Virchow recognized a *lymphatic* and *splenic* form of leukemia.

In the year 1868 the work of Neumann and Bizzozero on the hæmatopoietic function of the medulla of bone gave rise to a new field of clinical observation, and soon, a sufficient number of cases of leukemia were recognized in which profound changes in the medullary substance of the bone was present to warrant a third subdivision of the disease, namely: *myelogenic* leukemia.

Shortly after Virchow's description of leukemia, Boufils, Trousseau, Wunderlich, Wilks and others observed cases which presented extraordinary swelling of lymph glands and spleen and many of the clinical features of leukemia. It was noted, however, that the number of white blood corpuscles were not increased. In order to distinguish these cases from leukemia Trousseau proposed the name *adenia,* by which the French still recognize the disease. Wilks added that of *anemia lymphatica* or *Hodgkin's disease.* Wunderlich described it as *"progressive glandular hypertrophy."* Virchow as *lymphosarcoma,* Billroth as *malignant lymphoma* and Cohnheim as *pseudoleukemia.* Aside from the marked enlargement of the lymph glands and spleen the disease was characterized by pallor, hydrops, and a tendency to hemorrhages, cachexia, final marasmus and death. The cases did not include similar clinical manifestations due to malaria, syphilis or any other apparent cause. The essential feature which distinguished the affection from leukemia was the absence of the increase in the leucocytes. In many cases the lymph glands only were en-

larged. In other cases both the spleen and lymph glands showed marked increase in size. To the first class of cases the older writers applied the terms, *adenia, anemia* and *pseudoleukemia lymphatica.* To the second class was applied the terms *adenia, anemia* and *pseudoleukemia spleno-lymphatica.*

More recently a relatively small number of cases have been reported, belonging to this class of diseases in which the lymph glands were unaffected, while the spleen was greatly hypertrophied. These cases present a most striking analogy to splenic leukemia, the only difference being in the alterations in the blood. The number of cases thus far recognized clinically does not exceed twenty-five and the number of autopsies is still much smaller. The uniformity of the clinical and pathological features of the disease, however, establish the affection as a distinct morbid entity which is in reality a splenic form of pseudoleukemia.

In 1856, Woillez described the first undoubted case of this affection under the title, "Observations d' hyp. de la rate" (*Union Medicale*).

His report referred to a man 40 years of age, who was taken sick without apparent cause. The disease was characterized by anemia and a rapidly progressive course which terminated in death. There was no increase in the number of leucocytes. The spleen measured 26x12 cm. Two enlarged glands were found in the mesocolon.

The first case recognized as belonging to this type of disease was reported by Gretzel from Griessenger's clinic under the name of *Anemia splenica* (*Berlin Klin. Woch.,* 1866). Since the term *anemia splenica,* by which the disease under consideration has been most frequently reported, originated with this case, a brief review of its symptomatology and pathology may be of interest.

A child 10 months old, pale and weak from birth with

tendency to cough and diarrhea, presented a moderate enlargement of the liver and a great enlargement of the spleen. The lymph glands were large in many regions of the body. There was no leucocytosis. The disease gradually progressed, until at the end of six months the child died. Autopsy by Cohnheim showed hyperplasia of the normal elements of the spleen, incipient cirrhosis of the liver and general lymphatic hyperplasia.

Griessenger recognized that the case differed from leukemia solely in the absence of a leucocytosis. He among others, believed that such cases should be given a distinguishing name. Cohnheim had already applied the term pseudoleukemia to such affections (Virchow's Arch.. Bd. xxxiii) ; but Griessenger had accepted the term anemia lymphatica proposed by Wilks, as applicable to cases in which the lymph glands were chiefly involved. It was, therefore, natural for him to apply the term anemia splenica to similar cases in which the splenic enlargement predominated.

In reality the case described from Griessenger's clinic belongs to that pathological state described more revently by v. Jaksch as anemia infantum pseudoleukæmicæ.

Müller reported seven cases of pseudoleukemia (über idiopath. Milztumoren, Berlin klin. Woch., 1867). Among the number was one which undoubtedly belongs to the form splenic pseudoleukemia. Autopsy showed moderate enlargement of the liver and marked enlargement of the spleen. The splenic hypertrophy was due to an increase in its normal elements.

Under the name of *anemia splenica* Strumpell (Archiv. der Heilkunde, 1875) describes a case which has been quoted by nearly all who have written on the subject since that time. Banti claims that this was undoubtedly a case of progressive pernicious anemia. It certainly does not correspond to the disease, splenic pseudoleukemia.

To Banti (Dell anemia splenica archivo della scuola d' anat. pathologica, 1883) must be given the credit of

first describing the affection in such a manner as to bring the subject clearly before the medical profession. Unfortunately his publication was in Italian, which undoubtedly restricted its influence. He reported three cases, including two autopsies, from his own observations and collected cases previously reported, which he thought belonged to this class. He chose to perpetuate the term which Griessenger had applied to a somewhat similar condition and described the affection as "anemia splenica."

Since then cases presenting the same clinical manifestations and pathological features have been described under various names. Debove and Brehl applied the term splenomegalie primitive; Eichhorst, splenic pseudoleukemia; Gaucher, idiopathic hypertrophy of the spleen without leucocythaemia.

(For the report of other cases see references.)

The manifold nomenclature arising in part from the different theories regarding the nature of the disease, held by the different authors, gives rise to a certain amount of confusion in the literature concerning the affection.

At best the terms leukemia, pseudoleukemia and splenic anemia simply designate a certain grouping of clinical manifestations and pathological changes.

In the ordinary forms of Hodgkin's disease were frequently described as anemia lymphatica and anemia spleno-lymphatica, it would be consistent to apply the term anemia splenica to the rare cases under consideration. However, since the term pseudoleukemia is more often applied to such conditions I believe the appropriate name for the disease is splenic pseudoleukemia.

REPORT OF CASE.

Anton B., Russian, aged 45, was referred to my clinic at the Post-Graduate Medical School by Drs. Alex H. Ferguson and G. Burdick, April 16, 1898. The following history was obtained:

Family History.—Mother died of old age. Father died of unknown cause. No tuberculosis in family to his knowledge.

Personal History.—Never has had malaria nor has he lived in malarial district. Venereal disease denied. Wife and five healthy children and no miscarriages. The patient has not had typhoid fever or any illness, since grown. Has never used alcoholics. Came to Chicago nine years ago and has not lived outside the city since.

Was always strong and healthy. About three and a half years ago, patient noticed a swelling in the left hypochondriac region. The mass was firm but not painful on pressure or otherwise. At about the same time he also noted he was easily fatigued. Shortly after this he complained of slight nausea and he vomited occasionally. Appetite soon became impaired and has never been good since. At about the time the swelling in left side was first noticed the patient had diarrhea, three to four stools daily, which continued for nearly six months. Since then patient has been rather constipated. Has had chilly sensations now and then followed by fever. No distinct chill was ever experienced. This disturbance in temperature was not accompanied by pain or nausea and vomiting. Patient has complained of shortness of breath which has gradually increased from about the time the swelling was noticed. Now and then dizziness and headache has been present. Palpitation of the heart has not been noted. Pain on breathing has never been present. Epistaxis began about two years ago and since then has often been repeated. It has varied in amount from a few drops to a tablespoonful. Previously patient seldom had nose-bleed. Feet and ankles began to swell about one month ago and since then have not been free from swelling. Patient has noticed a gradual growth of the tumor in the left side. The greatest local discomfort, he describes as a feling of fullness and pressure in the epigastric and left hypochondriac regions. He has never experienced pain in any portion of the abdomen. He has lost about 25 pounds in weight and is not able to walk more than a very short distance without experiencing fatigue and dyspnea.

Physical examination.—Patient rather poorly nourished. Slight subicteric hue of skin and conjunctivæ. The mucous membranes show evidence of anemia. The skin and finger tips present the peculiar pallor of a moderately profound anemia. Ears and nasal cavities negative. Mouth and pharynx negative. Tonsils normal size. Glands at base of tongue not enlarged. Laryngoscopic examination, negative. The blood-vessels of the neck pulsate very distinctly. There are no glandular enlargements in cervical region. A small kernel is palpable in the right axillary region. The inguinal glands of both sides are very slightly enlarged—no more than often found in men. Edema of the lower extremities in moderate degre, extends

from feet to within a few inches below the knee on either leg. There is very slight edema at both wrists. Patient examined in the recumbent position, the costal arch in the left infraaxillary region is somewhat bulging and the left side of the abdomen appears distended with a uniform mass. A fullness is apparent in the epigastric region. On palpation, corresponding to the visible enlargement in the left half of the abdomen a firm mass is to be felt which apparently emerges from beneath the left costal arch. Its surface is smooth and its borders everywhere regular. The lower end of the structure is rounded and extends to within three finger breadths of the pubic bone. Below the umbilicus the mass extends an inch beyond the median line. One inch below the level of the umbilicus is a small depression or notch. Above, the inner border disappears beneath the costal arch in about the parasternal line. The left border of the tumor, beginning below, lies parallel with Poupart's ligament and above is indistinctly palpated in the lumbar region. One is able to grasp the lower pole as well as the inner border of the tumor. It moves with respiration in a diagonal direction and the mass permits lateral movement. Pain is not experienced on deep pressure or otherwise. The mass is continuous with a dullness which extends to the sixth rib in the anterior axillary line and the eighth rib in the posterior axillary line. Intestine is not to be demonstrated between the structure and the abdominal wall. All the requirements for the diagnosis of an enormous enlargement of the spleen are satisfied by the physical signs present in the case. Corresponding to the visible distension in the epigastric region, a uniform mass can readily be made out, which emerges from beneath the costal arch and sternum downward, within one and a half inches from the level of the umbilicus. From this point a very sharp regular border may be traced well into the lumbar region on the right side. In the mammary line the lower border is about a hand's breadth below the costal arch. The surface of this mass is smooth and firm and not painful on pressure. Accurate respiratory mobility in a direction parallel to the long axis of the body is present. The upper border of the liver is in its normal position. It is evident that the mass in the epigastric and right hypochondriac region is an enlarged liver. Upon auscultation over the spleen a loud bruit is everywhere to be heard. No friction rub audible over either the spleen or the liver. Slight ascites is present. There are no palpable retroperitoneal glands. The examination of the lungs aside from the dulness in the region corresponding to the enlarged spleen, shows few moist râles in infrascapular region of the left side. There is no increase in the size of the heart, on percussion. The apex beat is in the fifth interspace, just inside the mammary line. A faint systolic accidental murmur is heard over the base of the

heart. Genitals and rectum normal. Ophthalmoscopic examination shows no hemorrhage. No tenderness of the sternum or any other bones is present. The temperature at time of examination is normal.

One would not hesitate to make a provisional diagnosis of splenic leukemia on the history, signs and symptoms present in the case. With such findings the blood examination would rarely fail to corroborate the diagnosis.

Examination of the blood, April 17, 1898. Macroscopic appearance, blood very pale and thin. Coagulates slowly and imperfectly. Microscopic, fresh specimen: The red blood corpuscles show only slight differences in their size, form and color. No poikilocytosis. There is an evident paucity of cells. Rouleaux formation is absent. There is no increase in the fibrin. Leucocytes apparently not increased. Blood count:

Red blood corpuscles per cu. m.	1,740,000
White blood corpuscles per cu. m.	5,214
Fleischl	30 per cent.
Color index	0.86

Stained specimen: Neither nucleated red blood-corpuscles nor abnormal forms of leucocytes found.

Among 587 leucocytes the following relation of the different forms was observed:

	No.	Per cent.
Polynuclear neutrophile	390	66.4+
Eosinophile	5	.8+
Transformation forms	18	3 +
Large mononuclear	22	4 +
Small mononuclear or lymphocytes	152	25 +
	587	100

During the following two weeks, seven different examinations of the blood gave practically the same results as recorded in the first examination. The urine was negative. On April 25, 30 grams of grape sugar was administered which resulted in the production of alimentary glycosuria.

It is not necessary to enter into the details of diagnosis here, as they are given in the chapter devoted to that subject. Suffice to say, that without difficulty one would be able to exclude neoplasm and echinococcus cyst. No cause for amyloid degeneration is present. Under the circumstances a malarial cachexia is not to be seriously considered. The causes of cirrhosis of the liver are absent and the course of the affection has been unlike that of cirrhosis. The size of the spleen is greater than is found in that affection.

The history and physical examination correspond accurately to the clinical picture of splenic leukemia. In the absence of leukemia blood findings there is but one diagnosis to be made and that is splenic pseudoleukemia.

The patient came to the clinic from April 16 until May 7, when he was admitted to Cook County Hospital in the medical service of Dr. James B. Herrick, to whom I acknowledge my thanks for his kindness in allowing me to following the clinical features of the case until the patient's death. When admitted to the hospital the patient's condition had not materially changed from that on the date of the first examination, with the exception that he was somewhat weaker. Iron, arsenic and bitter tonics were administered and the patient remained in bed the greater part of the time. Appetite did not improve. Patient gradually lost strength and flesh. The temperature was normal with the exception of a slight rise now and then in the afternoon. Pulse rate ranged from 76 to 120. No discomfort was experienced. Pallor, edema and ascites gradually increased. There was a gradual reduction in the number of red blood corpuscles and in the amount of haemoglobin. July 7, a friction fremitus and rub was distinctly felt and heard over a small area of the liver in epigastric region. Pain was present over the same area. July 14, friction rub heard over all that portion of the liver exposed. Subcrepitant râles present in lower part of lung posteriorly. Temperature normal. Epistaxis now and then present. July 16, splenic puncture was performed and ten c.c. of blood was withdrawn (See experimental research). Blood from spleen was richer in leucocytes than the blood from the ear; but no abnormal elements found. Examination of the blood taken from the ear of patient July 17. An average of 768 squares gave red blood corpuscles 568,000;

white blood corpuscles, 8000; haemoglobin (Fleischl) 10 per cent.

No marked change in the size and form of the corpuscles. No nucleated red cells. No abnormal white corpuscles found. The normal relation of the different forms preserved. The slight increase in the white cells was due, no doubt, to an infection in the region of the parotid gland. A few days previous to the blood examination on July 17, a needle prick in the lobe of the right ear continued to ooze thin watery blood for more than one hour. No doubt infection took place at that point. July 28, abscess in parotid region drained. No temperature. Spleen apparently growing smaller. Friction rub disappeared from liver region. Involuntary evacuations began and continued until death. Patient gradually became weaker. Ascites increased. Dulness present over both lungs posteriorly. Condition of extreme marasmus present. Patient died August 17, 6:45 a. m.

AUTOPSY BY E. R. LE COUNT.

Time.—Three hours after death. Cadaver much emaciated. No rigor mortis. Skin and conjunctivæ subicteric. Opening in region of parotid gland from which pus is escaping. Absence of fat in abdominal wall. Diaphragm at sixth rib. Spleen extends to two inches below the crest of the ileum; anterior border on line of middle of the left rectus. Ascitic fluid present in large quantity. Liver extends to crest of ileum on right side. Both pleural cavities contain yellow fluid. Right pleura, slightly adherent at center of lung. Lungs: Right, no area of consolidation. Part of lower lobe non-crepitant. Contains icteric fluid. Left lung same as right. Peribronchial lymph glands not enlarged. Heart: Valves competent. Endocardium smooth and pale with ecchymoses beneath. Myocardium, firm, light colored, uniform in consistency and appearance. Aorta, negative with exception of slight atheroma. Retroperitoneal glands are small and pinkish and form a chain about the abdominal aorta. Section, firm and grayish-red, no softening, no yellow areas. Glands have appearance of true hyperplasia. Spleen: Weight, 2350 grams; 31x16x9.5. Smooth surface, bluish gray, small whitish areas diffuse in capsule. Section, red, firm and uniform. Wedge-shaped areas under capsule, which contain blood. Other white wedge-shaped areas with hemorrhagic

circumference. Malpighian corpuscles not visible, connective tissue apparently not increased. Kidneys, negative. Bladder and urethra negative. Adrenals, negative. Liver, weight, 2800 grams, 35x19x16x9 cm. Smooth outline, no adhesions. Section, lobular markings indistinct. Structure is uniform and firm, consistency not increased. Biliary apparatus negative. Pancreas, pale. Mouth, negative. Tonsils and glands at base of tongue, not enlarged. Larynx and trachea negative. Stomach: near pyloric end are a number of minute circular areas with elevated reddish centers presenting polypoid growths. Mucous membrane, pale. Small intestines pale. No enlargement of lymphatic apparatus of the intestine. Large intestine and rectum, negative. Messenteric glands slightly enlarged, no softening or yellowish areas. Skull, reddish pink, hemorrhagic character of diploea. Meninges, negative. Brain, negative. Glands of right axilla slightly enlarged and correspond to the description of the retroperitoneal lymph glands. Those of left axilla, enlarged although less in extent. In each groin, slight lymphatic enlargement resembling those about aorta. Bones, the whole length of the femur filled with dark red material, soft in consistency. The bony structure is lessened, corresponds to red marrow of foetal bone. Near the upper end of femur, an area of yellowish hemorrhagic tissue is rather sharply differentiated from surrounding softer and more red lymphoidal tissue. Same foetal condition of bone found in ribs, sternum and small bones of the feet. All the bones were fragile, due to the invasion of the compact tissue with lymphoidal or foetal bone marrow. In chest wall, right side, a small nodule is found under pectoral muscle between mammary and axillary glands. Although slightly fibrous in character it resembles most a lymphatic structure.

HISTOLOGY.

Spleen.—The majority of the Malpighian corpuscles show only slight alterations. Many appear normal, others present a slight increase in the reticular tissue and now and then a Malpighian body is found which shows considerable sclerosis. No marked degenerative changes are to be seen in the cells.

The veins show a moderate increase in the connective tissue which surrounds them. Areas are found where this increase is very marked. Fibrous tissue extends some distance into the splenic pulp, enclosing within its meshes lymphoidal cells, isolated and in group. (See Fig. 1.)

In many places, the pulp appears normal, however, in general it is apparent that the reticulum is considerably increased. Now and then are to be found areas of marked sclerosis containing lymphoidal cells in the meshes of the fibrous tissue. (See Fig. 2.) Nowhere

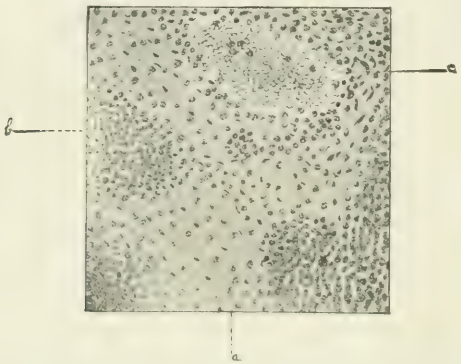


Fig. 1.—a, connective tissue invading pulp; b, group of lymphoidal cells surrounded by connective tissue; c, splenic vein.

in the spleen are signs of acute inflammation or marked degeneration of cells to be found. Section through in-

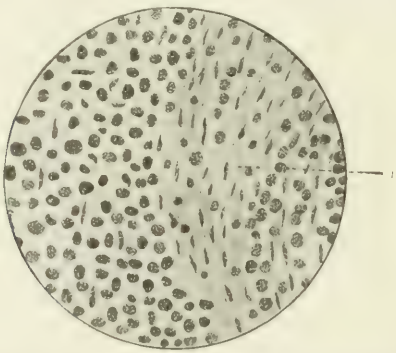


Fig. 2.—Splenic pulp, showing area in which the recticulum is fibrous. a, lymphoidal cells.

farcted areas in the spleen shows nothing more than is usually found.

Liver.—The liver shows a slight increase in the interlobular connective tissue with marked infiltration of lymphoidal elements between the lobules and liver cells.

(See Fig. 3.) The cellular infiltration resembles somewhat that found in leukemia. Considerable granular pigment is present.

Lymph glands.—The slightly enlarged retroperitoneal

Fig. 3.—Liver.

mesenteric inguinal and axillary glands present hyperplasia of both connective tissue and lymphoidal elements. The connective tissue, however, shows the greater increase. Fibrous bands surround lymphoidal

Fig. 4.—Fibrous hyperplasia of inguinal gland.

areas and the lymph cells are separated by a visible reticulum. The inguinal glands show much more connective tissue increase than any of the others. They present a condition of real fibrous hyperplasia. (See Fig. 4.) The retroperitoneal, mesenteric and axillary

glands are practically alike in their histology. The hyperplasia of the connective tissue is not nearly as marked in the inguinal glands. (See Fig. 5.)

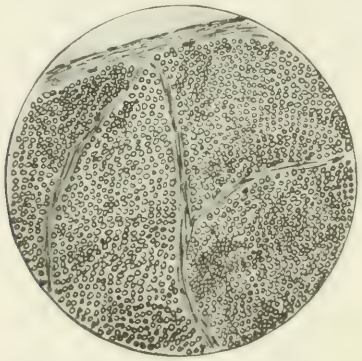


Fig. 5.—Retroperitoneal lymph gland.

Bone marrow.—The medulla of the femur which was similar in macroscopic appearance to that found in the other bones is made up of lymphoidal cells arranged in groups or singly, contained in a fine network of connective tissue. Here and there were areas in which capillary spaces containing blood corpuscles predom-

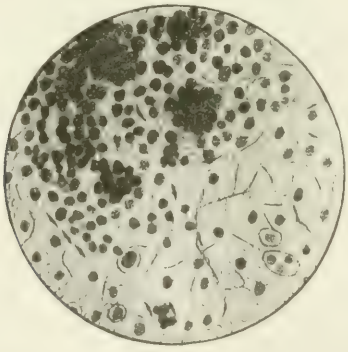


Fig. 6.—Bone marrow of femur, showing fetal condition.

inated with an occasional lymphoidal cell contained within the network of capillary walls. (See Fig. 6.) Erhlich's stain reveals nucleated red blood corpuscles.

The lymphoidal area found in the femur previously described in the macroscopical appearance is made up of lymphoidal cells arranged either in groups or singly surrounded by a reticulum of finely fibrillated connective tissue much greater in amount than in the medulla. Blood-vessels with distinct walls permeated the structure; but no aggregation of capillaries, such as described in the medullary tissue is to be found. (See Fig. 7.)

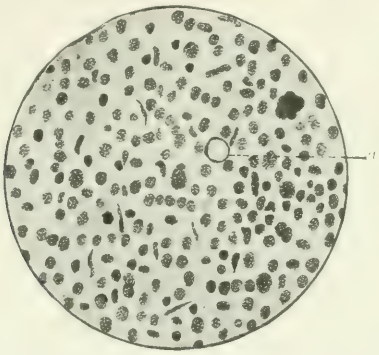


Fig. 7.—Lymphoidal area in medulla of femur; a, blood vessel.

The polypoid growth in the stomach showed a proliferation of the normal glandular structures containing in it areas of round cell infiltration. Projecting into the center of its growth is fibrous tissue rich in blood vessels. The small tumor in the thorax is made up of fibrous tissue which contains within its meshes lymphoidal cells. The heart muscle shows slight granular degeneration.

Lungs.—Negative; parotid gland, adrenals and pancreas negative.

EXPERIMENTAL RESEARCH.

It is believed by many investigators that both leukemia and pseudoleukemia are due to some form of infection. The nature of the infection is not always specified. Some regard the infective agent as a micro-organism. According to Grawitz twenty-nine cases of pseudo-

leukemia have been reported in which bacteria have been found in the swollen glands. Recently Delbet claimed to have cultivated a bacillus from the spleen in a case of pseudoleukemia and that inoculation of dogs with this micro-organism resulted in the production of glandular swelling.

For the reasons stated in the chapter on theory regarding origin and nature of pseudoleukemia, it seems probable that the disorder is located primarily in the spleen and that the anemia and cachexia are in some way secondary to the splenic affection.

Ante-mortem Research.—With a view of determining, if possible, whether micro-organisms or other toxic agents were present in the spleen, on July 16, after most careful preparation, 10 cu. c. of blood was aspirated from that organ. Tubes containing the following media were inoculated: Glucose and lactose bouillon, milk, human blood serum, Lœffler blood serum, glycerine agar, nutrient agar and gelatine. The spleens of a guinea-pig and rabbit were inoculated through a laparotomy incision. The tubes remained sterile, with the exception of the one containing human blood serum. Upon this a coccus developed which proved to be the staphylococcus pyogenes aureus. On the third day after inoculation, the guinea-pig showed a portion of gut protruding from the anus which became gangrenous, resulting in death in three days. Organs, sterile and histology of spleen normal. August 3, rabbit died and autopsy by Dr. G. Wells showed stomach enormously distended with food and signs of hemorrhagic gastritis. Spleen and liver normal size. Other organs, negative. Histology of spleen and liver negative.

Post-mortem Research.—Autopsy, three hours after death. The same kind of culture media was used as in the ante-mortem experiment. The tubes were inoculated from the spleen, liver, bone marrow and blood from the heart. On an agar tube inoculated from the

spleen, a bacillus developed, which subsequently satisfied the requirements of the bacterium coli commune. Ordinary staphylococci developed on a tube of blood serum. Another blood serum tube, inoculated from the liver developed the bacterium coli commune. All the other tubes were negative. An emulsion was made by macerating a small portion of the spleen in about four times the quantity by weight of sterilized water. The emulsion was carefully filtered and three full grown rabbits and two guinea-pigs were inoculated with the filtrate. The veins of the ears of two of the rabbits were injected each with 2 cu. c. of the extract. Both rabbits died during the following night. Cultures from the heart blood were negative. The intravenous injection of mice with the blood of the rabbits proved negative. Autopsy on rabbits showed no apparent cause of death. The histological examination of lungs, spleen and liver of both rabbits was negative. Five cu. c. of the same filtrate was injected into the peritoneal cavity of a guinea-pig which lived until September 12. During the last two weeks the animal showed signs of emaciation. Unfortunately the autopsy was not held until twelve hours after death. The bacterium coli was found in the heart blood. Peritoneum and organs showed neither macroscopic nor ' microscopic changes. The spleens of a guinea-pig and rabbit were inoculated with a portion of the same filtrate with negative results.

Conclusions.—The staphylococcus found in the experiment performed ante-mortem may have been located in the skin. The staphylococcus derived from the spleen from the inoculation made post-mortem may readily be explained on the grounds that just previous to death a suppurating wound was present in the parotid region. The presence of the colon bacillus in the spleen and liver, after death from marasmus, is not surprising. The cultivation of the colon bacillus from the blood of the heart of the guinea-pig twelve hours

after death is irrelative. No micro-organisms were found in the microscopic section of the tissue of the spleen or any other organ. The inoculation experiments performed both ante-mortem and post-mortem were negative as regards the finding of a specific micro-organism. The death of the two rabbits so soon after the intravenous injection of an aqueous extract of the spleen renders it very probable that an abnormal toxic substance of some nature was present in the organ. Whether that toxic substance had been produced throughout the course of the disease and whether it was responsible for the anemia and general malnutrition in the disease is in the light of our present knowledge mere speculation.

ETIOLOGY.

The etiology of splenic pseudoleukemia is unknown. The disease does not appear to bear any direct relation to malaria, syphilis, tuberculosis or alcoholism. It seems to arise independently of all constitutional disorders. The cultures obtained from the spleen in my case both ante-mortem and post-mortem contained no organism that could be regarded as specific, and the spleens of animals injected with blood from the spleen of the patient showed no changes. The microscopic examination of the spleen and other organs revealed no micro-organisms. In 1894 Sciolla obtained negative results from cultures made from the spleen ante-mortem. The negative results in the two cases mentioned does not, of course, exclude micro-organisms as a cause of the disease. However, certain features in connection with the disorder render it very improbable that a specific micro-organism is the etiological factor. The disease is extremely rare and has never occurred endemically or epidemically. Isolated cases have appeared in different parts of the world. More cases have been recognized in Italy than in any other section.

There appears to be no special predisposing cause of the disease.

PATHOLOGICAL ANATOMY.

I find record of only about ten post-mortems in which it is reasonably certain that splenic pseudoleukemia was the cause of death, and in some of these the reports are very meagre.

As a rule the cadaver presents a high grade of emaciation. In some cases the subcutaneous fat has been well retained. The skin and conjunctivæ are subicteric and punctiform hemorrhages may be visible in different parts of the body.

Usually the subcutaneous connective tissue of the dependent parts is infiltrated with serum, and edema of the extremities is often present. Visible external glandular enlargement is seldom found; yet it is not rare to be able to palpate a few glands the size of a bean or a hazel-nut in the inguinal or axillary regions. The abdomen usually contains a variable quantity of ascitic fluid. Ecchymoses may be present beneath all the serous surfaces. The pericardial sac often contains a serous fluid. The heart is generally slightly dilated and frequently presents signs of granular and fatty degeneration of its muscle such as is usually found in severe anemia. The pleural cavities often contain fluid and when the spleen is extremely large, compression of the left lung may give rise to atalectasis of its lower lobe. In a few cases a pleurisy has been present on the left side. Although nausea, vomiting and diarrhœa may be prominent symptoms throughout the course of the disease, the gastro-intestinal tract does not present serious alterations. The glands at the base of the tongue have been found somewhat enlarged. Not infrequently Peyer's patches and the solitary follicles show slight hyperplasia.

The liver is usually enlarged. In my case it weighed 2800 grams, which exceeds by far the usual weight re-

corded in this affection. Its surface is smooth, edges round, and the organ presents, as a rule, no visible signs of cirrhosis. On section, the organ is uniform in firmness, cuts easy and its consistency is not apparently increased.

Histology of the Liver.—The liver shows slight increase in its interlobular connective tissue. Infiltration of the round cells is observed about the portal vessels and between the liver lobules. In a case reported by Banti there was considerable increase in the connective tissue, which he described as an interstitial perilobular hepatitis. The liver cells may be normal. Here and there is considerable proliferation of connective tissue, the hepatic cells may be atrophic.

The spleen is always increased in size and often fills the greater part of the left half of the abdominal cavity. The normal size of the spleen is 12x8x3 cm. Its normal weight is 200 grams. In my case it measured 31x16x 9.5, and weighed 2350 grams. The normal shape and outline of the organ is preserved. Its surface is usually smooth, although in some cases, areas of peritoneal thickening resulting from perisplenitis are present. Rarely, peritoneal adhesions have been recorded. The organ is firm. In a case reported by Banti there was a visible increase in the connective tissue. Small white areas, about the size of a pea, were noted by him which proved to be made up of increased connective tissue. In my case there was no macroscopic increase in the connective tissue. The Malpighian corpuscles were not visible.

Histology of the Spleen.—The Malpighian corpuscles are usually not markedly altered. Banti records considerable sclerosis of these bodies in one of his cases. He summarized his findings in the spleen, as, 1. Atrophy and sclerosis of the Malpighian corpuscles. 2. The substitution of an irregular and fibrous reticulum for the normal fine reticular substance of the splenic pulp.

The following quotation is from a case by West: "The spleen showed slight increase in the trabecular tissue i. e., slight fibrosis. Malpighian corpuscles are much diminished in size and badly developed. Iron reaction negative." For the changes in the spleen in my case the reader is referred to the histology given in the report.

The kidneys are anemic. The epithelium of the tubules may show signs of granulo-fatty degeneration. A real nephritis, however, is not present. The pancreas and adrenals are negative. The lymphatic glands are usually not enlarged. In some cases, however, isolated glands or small groups of glands, especially in the retroperitoneal region, have shown slight enlargement. They are grayish-red and somewhat firm in consistency. On section, they show no softening and the microscope reveals hyperplasia of both the principal elements. The mesenteric glands may show similar changes.

The medulla of the bone often presents an appearance closely resembling that found in primary pernicious anemia. In one of Banti's cases he notes that the medulla in the long bones was, as a rule, fatty, but that in both femora, a fœtal condition of the marrow was present. In my case the compact tissue of all the bones was very much reduced, producing a degree of brittleness. The sternum could easily be broken with the fingers. Throughout the length of the femur, tibia and humerus the normal fat was replaced by dark red marrow. Indeed, red atrophy of the marrow was distinctly present in every bone examined, including, besides those mentioned, the ribs, clavicle, skull, vertebræ and small bones of the feet.

The blood changes found in the disease are discussed under the heading of symptomatology.

SYMPTOMATOLOGY.

The following description of symptoms is based on

those present in my case, supplemented by a study of the cases most carefully reported.

The manner of onset varies. As a rule, however, the disease begins very insidiously, so that it is often difficult to establish the period at which the first manifestations of the affection appeared. In many cases the first symptoms noted are cardiac palpitation on exertion, accompanied by a feeling of unusual muscular fatigue. Headache and slight pallor of the mucous membranes may be present. Early in the disease the appetite and digestion are usually good and the bowels regular. After a period varying from a few weeks to two or three months, the attention of the patient is attracted to the existence of a tumor in the left hypochondriac region. The tumor is seldom painful and disturbs the patient chiefly by a sense of weight and tension in that region. In some cases, as in my own, a tumor in the left hypochondriac region is the first symptom noted by the patient. Shortly after this discovery, owing in part, no doubt, to the mental concern of the patient in regard to his disorder, a feeling of weakness on muscular exertion is experienced. Following this may appear nausea and vomiting, and at times persistent diarrhœa. Dyspnœa and cardiac palpitation on exertion may be rather prominent features. Now and then dizziness and headache may be experienced. Epistaxis is a common early symptom.

In other cases a tumor may appear in the left hypochondriac region which may increase in size for nearly a year without any disturbance in the general health, or even local disturbance, aside from a feeling of weight or tension in the part. After a variable time, seldom longer than a year, the symptoms of anemia and general disturbances in organic function supervene.

In rare cases, as in one reported by Debove, the local phenomena referable to the spleen may be very distressing. Pain, paroxysmal in character, simulating

hepatic colic, with attacks of nausea and vomiting may accompany the gradual loss of muscular power and signs of anemia. Examination of the patient may then reveal the signs of marked anemia and a palpable tumor in the left hypochondriac region.

It matters not what the mode of onset is; after the disease has developed, the clinical picture will present the same essential features, viz.: 1. Hypertrophy of ment. 3. Anemia progressing toward a cachectic state. ment. 3. Anemia progressing toward a cathectic state. At this time the symptoms are all very pronounced, with the exception of pain, which may be only slight or entirely absent throughout the whole course of the affection. Debility is great. Edema appears, at first transitory in character, involving the ankles and wrists. A vespertine fever preceded by chilly sensations may be present. Gastro-intestinal disturbances manifested in anorexia, indigestion and diarrhœa are present in varying degrees of intensity. Finally within a period of a few weeks or months, the cachexia of anemia becomes pronounced. Emaciation gradually increases. The skin and conjunctivæ become subicteric. Pallor peculiar to profound anemia appears. Muscular weakness confines the patient to his room or bed. Edema becomes permanent and is associated with ascites and hydrothorax. Petechial hemorrrhages in the extremities and mucous membranes evidence the high grade of malnutrition of the capillary walls. Persistent and often incoercible diarrhœa exhausts the patient and involuntary evacuation of the bowels may announce the approach of dissolution.

At the beginning of the cachectic stage the blood examination usually shows a grade of anemia which approximates very closely the findings in chlorosis. As the cachexia increases, the number of red blood corpuscles, as a rule, diminishes, until finally, as in my case, less than one million per cubic millimeter may be reg-

istered with hæmoglobin so slight in amount as to preclude the possibility of accurate estimation. At no time, however, is there a leucocytosis presenting the characteristics found in leukemia. From a scientific as well as a therapeutic standpoint, it is extremely interesting to note that so far as may be gleaned from the histories, the splenic hypertrophy has preceded, or at least has developed contemporaneously with, the appearance of the anemia. In no case properly belonging to this type of disease, so far as I have been able to discern, has the splenic hypertrophy followed the appearance of the anemia. In the majority of cases the patient has not consulted the physician until his attention has been attracted to the tumor in the side. In my case, the patient, naturally a quick observer, was not conscious of any unusual physical manifestations until he discovered a tumor a few inches below the costal arch in the left hypochondriac region.

The fact that splenic hypertrophy is apparently the primary condition has an important bearing on the therapy of the disease. It also contributes much to the nature of this type as well as the other forms of pseudo-leukæmia. As a rule, in the progress of the disease the size of the spleen bears a direct relation to the grade of anemia. However, there are exceptions, in which the spleen is enormously enlarged before anemia is pronounced. In still other cases anemia may be profound when the splenic tumor is of moderate size. After cachexia develops the disease is usually rather rapidly progressive and death is due to complications or follows a period of extreme marasmus.

The disease may be divided into three stages. The first stage includes an indefinite period during which the spleen begins to enlarge. The second stage may be conveniently said to include that period during which the symptoms of anemia develop, accompanied, as a rule, by gastro-intestinal disturbances and general asthenia.

The third stage is that of cachexia. This stage is usually ushered in with edema, followed by a somewhat regularly progressive aggravation of all the symptoms of the previous stages, and finally terminates in extreme marasmus and death.

Special Symptoms: Splenic Hypertrophy.—So far as known, all disorders of the spleen of clinical importance are accompanied by its enlargement. Splenic pseudoleukemia presents as one of its essential features an enlargement of the spleen. The enlargement is uniform, constituting a true hypertrophy in a clinical sense. Its size varies with the stage of development of the disease and is not the same in all cases. The spleen enlarges gradually and is not subject to marked fluctuations in size. Owing to the fact that the first stage of splenic enlargement is seldom observed it is impossible to estimate its rapidity of growth from the beginning. In my case, after the spleen was first palpable, it gradually enlarged until its lower border reached a point two fingers' breadth above the pubic bone and its inner border extended beyond the median line, patient in the upright position. In this case the enlargement was exceptionally great. As a rule, the organ extends no farther than one or two hands' breadths below the costal arch. Usually, no irregularities are to be felt either on its margin or surface. Its consistency is firm. The splenic notch occupies its usual position. The organ is respiratory movable in the diagonal direction peculiar to splenic enlargements and permits lateral movement. Pain on pressure may or may not be present. In my case a loud soufflé was to be heard all over the enlarged organ. In some cases friction rubs, due to perisplenitis, have been heard. A perisplenitis may result in a local thickenings that may be felt as irregularities on the surface of the organ. When the enlargement is marked the left half of the abdomen is more prominent than the right, and region of the left costal arch appears bulging.

In my case, just previous to death and at the time of great diarrhœa and involuntary discharges, the spleen reduced fully two inches in its various diameters. The enlargement of the spleen may be unaccompanied by pain. In the majority of cases an uncomfortable sensation of weight and fulness in the left hypochondriac region leads to the discovery by the patient of the tumor. In rare cases, neuralgic pains or paroxysms resembling hepatic colic accompanied by obstinate vomiting appear as early manifestations of the disease. At times the pain may be so intense as to demand radical means for its relief. The explanation of the pain is not always apparent. A perisplenitis is often found, but pain has been a marked feature when such a condition was not present. In all cases when pain exists it is increased by pressure.

Lymph Glands.—The lymph glands may remain normal in size throughout the course of the disease. It is not uncommon, however, for post-mortem to reveal slight enlargement of the retroperitoneal and bronchial glands either isolated or in groups. In a few cases after splenic hypertrophy has existed for a long time and the symptoms of the disease were well developed small kernels have appeared in the axillary and inguinal regions. The glands at the base of the tongue and the tonsils have been found enlarged.

Anemia.—Anemia is one of the most characteristic features of the disease. So far, it has not been recorded in any case that the signs of anemia preceded the development of splenic hypertrophy. The symptoms of anemia develop gradually during the second stage of the affection until that state of profound alteration of general nutrition is reached, which is clinically designated by the term, cachexia. During this stage dizziness, tendency to syncope, headache, dyspnœa on exertion and cardiac palpitation are present in variable degrees of intensity. Pallor of the mucous mem-

branes develops. Hæmic heart murmurs may be heard. The skin assumes a hue peculiar to anemia—pallid at first and later on of a yellowish tinge. The conjunctivæ become slightly subicteric. Epistaxis, such as may occur in anemia from any cause, is often a frequent and early symptom. The hemorrhage is seldom profuse. The advent of cachexia is characterized by a tendency to edema and effusion into serous cavities, marked asthenia, hemorrhages, fever and an aggravation of all the pre-existing symptoms. The mucous membranes become exceedingly pale. The patient gradually emaciates. Persistent diarrhœa often supervenes in the later stages and anemia progresses to the highest degree. A period of extreme marasmus finally terminates in death.

The *cachexia* of splenic pseudoleukemia does not differ from the cachexia of carcinoma, tuberculosis, or any other profound disturbance of nutrition. Though epistaxis is frequently an early symptom, hemorrhage from other organs than the nose seldom takes place until cachexia develops. During this stage hæmatamesis, hæmoptysis, melenæ and hæmaturia have been observed, and petechia of the skin and mucous membranes is common. Retinal hemorrhages are to be expected.

Temperature.—Fever may be present during the early stages of the affection. It is a variable symptom and may be absent for weeks at a time and then irregular pyrexia may develop. It may be due to a localized peritonitis. Pyrexia independent of local causes is seldom pronounced until the stage of cachexia, when from time to time an afternoon temperature of 102 may be registered. The fever is similar to that which is present in leukemia and all grave anemiæ. No satisfactory explanation has ever been given for its occurrence.

Liver.—The liver is nearly always considerably enlarged. Its surface and outline is regular; its con-

sistency firm, and its lower border sharp. Periphepatitis may occur.

Circulatory Symptoms.—The heart may be slightly dilated. Hæmic murmurs are often heard, especially in the later stages. The carotids and other large arteries throb visibly and a capillary pulse may be present. The pulse is full and frequent and may approach the water hammer character. The veins are often prominent and the *bruit diable* may be heard in the neck.

Pulmonary Symptoms.—Râles due to compression of the lung by the splenic tumor are often present at the base of the left lung. Dyspnœa due to deficient hæmoglobin and the elevation of the diaphragm is experienced.

Digestive disturbances.—As a rule the appetite is fair until the disease is well advanced, when it gradually fails. Nausea and vomiting may be early symptoms, and when associated with paroxysms of pain in the region of the spleen, may cause much distress. The gastric disturbances may be due to pressure or possibly may be reflex through involvement of the sympathetic nervous system. Diarrhœa may be an early symptom and persist for several weeks or months. Constipation often alternates with diarrhœa. Toward the end, diarrhœa may be incoercible, and at last involuntary evacuations may take place. Hemorrhage from the stomach has been recorded.

Nervous System.—The symptoms referable to the nervous system are those chiefly of anemia, namely: vertigo, headache, neuralgia and mental fatigue. The mind usually remains clear until near the end.

Blood.—The blood varies with the stage of the disease. In the beginning of the affection there is only a slight reduction in the number of red blood corpuscles and a relatively greater diminution in the hæmoglobin. After the disease is well advanced the blood is very pale and thin. Its coagulability is very much reduced.

Red blood corpuscles: The red blood corpuscles are, as a rule, very much diminished in number. In a few cases in which they have been counted the number has ranged from 4,000,000 to 568,000 per cu. m.

The average case will show about 2,500,000 per cu. m. at the beginning of the stage of cachexia. As the disease progresses the number usually decreases. There is no marked change in the size and form of the corpuscles. Nucleated red blood corpuscles have not been observed. Roulcaux formation is absent in the later stages.

The hæmoglobin is reduced in quantity. The individual corpuscle contains less than the normal amount of hæmoglobin. The color index, however, does not seem to be as low as in chlorosis. In my case, although the hæmoglobin was reduced to 10 per cent., the color index was never lower than about 85 per cent.

White blood corpuscles.—In the majority of cases the leucocytes are normal in number and the relation of the different forms is not disturbed.

No abnormal elements have been recorded. In one of Banti's cases the number was increased to 19,805 per cu. m., but pneumonia was present as a complication.

In Franzolini's case, five times the normal number of leucocytes were found. Under such circumstances the character alone of the leucrocytes would enable one to differentiate the disease from splenic leukemia.

Urine.—The urine is normal in quantity and may not show special changes. A large quantity of nucleohiston was found by Stein in a clinical case of splenic pseudoleukemia. The solids of the urine are not altered in a characteristic manner. A trace of albumin has been found. Signs of extensive degenerative changes in the kidney have not been observed. Sugar is absent. I was able to produce alimentary glycosuria by administering a moderate quantity of glucose. This was

probably due to impairment of the function of the liver.

DIAGNOSIS.

Essential to the diagnosis of splenic pseudoleukemia is: 1, an idiopathic splenic hypertrophy; 2, a progressive anemia without a leucocytosis presenting the characteristics found in leukemia; 3, the absence of marked lymphatic enlargement.

Since neither signs of anemia nor local sensations have been noted previous to the development of splenic hypertrophy the disease could scarcely be suspected before the spleen was palpable. In relation to splenic hypertrophy one must determine whether the palpable structure in the left hypochondriac region is a splenic tumor and if so, its nature. As a rule, tumors of the spleen present less difficulty in diagnosis than those of any other abdominal structure. They emerge from beneath the left costal arch and cling closely to the abdominal wall overriding all structures in the abdominal cavity. Their development is downward along a line which is directed toward the right pubic bone. Splenic enlargements are respiratory movable and in a diagonal direction which is peculiar to splenic tumors. All other structures attached to the diaphragm have a tendency to move in a line parallel with the long axis of the body. A variable degree of lateral motion is permitted. The structure is uniform in consistency, outline and surface, which constitutes a true hyperplasia in the clinical sense. Unless the spleen is dislocated it is impossible to grasp its upper margin; but the palpating finger rests on a smooth surface which seems to be a part of a structure which extends upward beneath the costal arch. Its inner and lower margins are readily palpated and the lower pole may often be grasped, which is characteristic of splenic enlargements. The inner margin is notched. The dullness on percussion over the structure in the abdominal region is continuous with that of a uniform dullness in the splenic region extending often to the

eighth rib in the post-axillary and the sixth rib in the anterior-axillary line.

Tumors of the kidney are usually fixed, and their development from the lumbar region is evident on bimanual palpation. They develop as a rule downwards and seldom encroach upon the diaphragm. Urinary symptoms are often present and the colon may be demonstrated as lying in front of the kidney mass.

Enlargement of the left lobe of the liver may present some difficulty in diagnosis. Under such circumstances the direction of the respiratory mobility and above all the continuity of its lower border with the lower border of the liver in the epigastric region would serve as distinguishing features.

Having determined that the mass in the left hypochondriac region is a splenic structure the nature of the enlargement must next be considered. It is characteristic of splenic hyperplasia in that the form and outline of the normal spleen is retained. A neoplasm such as carcinoma of the spleen is to be excluded, or at least can scarcely be diagnosed in the absence of irregularities in the structure. Acquired syphilis rarely produces great enlargement of the spleen in the early stages of the disease, and still more rarely as a tertiary manifestation, excepting when combined with amyloid degeneration. The history, presence of amyloid elsewhere and other signs of syphilis would render the diagnosis easy. Enlargement of the spleen from tuberculosis would rarely present any difficulty in diagnosis. Echinococcus of the spleen is to be distinguished by its long course without general symptoms and the presence of fluctuation. In case of doubt, puncture would clear up the diagnosis.

After having excluded all forms of neoplasm and cyst a hyperplasia of the spleen may be assumed. Its nature would then require careful consideration. A differential diagnosis should be made between the morbid states, which are accompanied by a splenic hyperplasia, namely,

splenic leukemia, malarial cachexia, passive congestion, progressive pernicious anemia, amyloid spleen and Banti's splenomegalia with hepatic cirrhosis.

Splenic leukemia: The clinical phenomena are so nearly identical, in the two affections, that a blood examination shows the only essential difference between them. A moderate increase in the polynuclear variety of leucocytes may be present in splenic pseudoleukemia. In one of Banti's cases there was an absolute leucocytosis, but the blood examination was not made until the day upon which a pneumonia developed. In this and in a few other cases in which a moderate leucocytosis has been present, the quality of the leucocytes has not been accurately stated. In the diagnosis of leukemia when leucocytosis is only moderate the quality of the leucocytes, not their number, determines the diagnosis. Essential to the diagnosis of leukemia with moderate leucocytosis is the increase in the mononuclear elements which often show degenerative changes in their nuclei. As a rule in splenic pseudoleukemia there is a normal number of leucocytes and the relation of the different forms is not disturbed. The number of red blood-corpuscles is at first moderately reduced. Later in the disease the number may be diminished to two million or one million, or as in my case to a little more than half a million per cubic millimeter. Change in the size and form of the red blood-corpuscles is not marked. The individual red blood-corpuscles are poor in hemoglobin, and rarely contain nuclei. A more extended account of the blood in splenic pseudoleukemia is to be found under symptomatology. The differential diagnosis between the clinical pictures, presented by splenic pseudoleukemia and splenic leukemia is to be made only by a study of the white blood corpuscles.

Malarial cachexia: The form of malaria known as malarial cachexia characterized by enlargement of the spleen and anemia presents clinical phenomena very

closely simulating splenic pseudoleukemia. Splenic hypertrophy, enlargement of the liver and anemic cachexia are essentially the same in both affections. Indeed, it must be admitted that a positive differential diagnosis between the two conditions could not be made under certain circumstances. As a rule, however, the differential features are sufficiently prominent to leave no doubt as to diagnosis. In all cases, so far reported which are to be included in the category of splenic pseudoleukemia, malaria has been carefully excluded as an etiological factor. A malarial cachexia developing as it sometimes does in intense malarial districts without chills, would present features requiring great care in diagnosis. The presence of the plasmodium in the blood would of course be conclusive evidence as to the nature of the disease. Blood pigment in the white blood-corpuscles, or free in the plasma, has not yet been noted in quantities approaching that found in malarial cachexia. The pigmented skin is a slate or dirty yellow color, peculiar to chronic malaria. In splenic pseudoleukemia pallor is combined with subicterus. In districts where malaria is intense, a nephritis not infrequently complicates the disease, while it has never been noted in cases of splenic pseudoleukemia. The temperature and absence of chills may be alike in both affections. Inhabitants of a malarial district who have never had the usual manifestations of malaria, as well as those who unquestionably have suffered from the disease, may develop splenic hypertrophy, which often persists for a long time, even a period of years, without the appearance of anemic cachexia or serious disturbance in general health. Splenic pseudoleukemia is characterized by a splenic hypertrophy which is directly associated with or very soon followed by a progressive anemia which invariably continues to cachexia with fatal termination in a definite period of time unless the disease is arrested. The therapy, which

in time will relieve a malarial cachexia, has no particular effect on splenic pseudoleukemia.

Essential anemias: In chlorosis the blood findings and clinical phenomena of the early course of the disease may be very similar to those of splenic pseudoleukemia. However, in chlorosis the splenic enlargement is absent or seldom marked and when present follows rather than precedes the development of the anemia. The course and effect of treatment in the two affections is entirely different. In primary progressive pernicious anemia the cachexia, course and clinical phenomena in the two diseases resemble each other in many particulars, but the blood findings and splenic hypertrophy present differences sufficiently great to establish the diagnosis. In primary progressive pernicious anemia, the individual corpuscle is relatively rich in hemoglobin, while in pseudoleukemia it is poor. There is a much greater difference in the size and form of the red blood corpuscles in primary progressive pernicious anemia. Nucleated red blood corpuscles are rarely, if ever, found in the splenic pseudoleukemia, while they are constantly found in primary progressive pernicious anemia. The presence of the large form of nucleated red blood-corpuscle, the gigantoblast, of especial importance in the diagnosis of primary progressive pernicious anemia, has never been found in splenic pseudoleukemia. In primary progressive pernicious anemia the spleen is more often atrophied than enlarged. The enlargement, if sufficient to be detected on palpation, is never great, usually shows fluctuation in size under treatment, and always follows the development of anemia. Mosler and Gast believe the enlargement of the spleen in chlorosis and primary progressive anemia to be a compensatory hypertrophy directly connected with the regeneration of the blood. Other authors, as Immermann, Eichhorst, Müller and Neumann, do not believe that under such circumstances the spleen returns to its prenatal hema-

topoietic function. By others the splenic enlargement in the anemiæ is thought to be due to the increased destruction of red blood-corpuscles. The liver is nearly always hypertrophied in splenic pseudoleukemia. In primary progressive pernicious anemia it is not.

Passive congestion of the spleen: In this condition the etiological factors of a liver cirrhosis or other conditions inducing splenic hyperemia would be present. The course of the two diseases is somewhat different. The development of anastomoses between the portal and general circulation and the other signs of liver cirrhosis such as early appearance of ascites and late appearance of cachexia characterize the spleen of passive congestion. The enlargement of the spleen in passive congestion is moderate in comparison to the enormous hypertrophy sometimes present in splenic pseudoleukemia. In atrophic cirrhosis, the liver is small while in splenic pseudoleukemia it is hypertrophied. On the other hand cirrhosis of the liver accompanied by marked fatty infiltration and enlargement of the organ presents clinical features, which under certain circumstances, might give rise to great difficulty in diagnosis.

Amyloid spleen.—The diagnosis of amyloid spleen is to be made only when a sufficient cause has preceded its development, such as long continued suppuration of bone or soft parts, phthisis pulmonum or protracted syphilis. Evidence of amyloid degeneration elsewhere is to be desired in connection with its etiology. Although the spleen is usually the first organ to show amyloid changes the diagnosis of amyloid hyperplasia without signs of amyloid liver, kidneys or intestines would be at best a probable diagnosis.

Splenomegalie with cirrhosis of the liver.—Banti (*Semaine Med.*, 1894, xiv, 318 and Ziegler's Beiträge 1898) describes a condition characterized by splenic hypertrophy associated with cirrhosis of the liver in which he believes the primary disease is of the spleen

and that the cirrhosis of the liver results from the pathological changes in the spleen. The clinical difference between the two affections is so slight that Banti admits that on that alone no distinction between the two affections can be made.

The diagnosis of splenic pseudoleukemia is often surrounded by many difficulties. In all cases, the evidence must be accurately obtained and the proper valuation placed on it to insure trustworthy results. Undoubtedly there are cases in which it would be advisable to withhold a positive diagnosis for a variable period of time.

COURSE AND PROGNOSIS.

The disease presents a definite course within certain limits of variation. Its tendency is distinctly progressive. The severity of symptoms may show slight remissions, but on the whole, it will be observed that the patient loses ground rather steadily from month to month. It is difficult to estimate the exact duration of the disease, owing to the uncertainty connected with the length of the first stage. In some cases a fatal termination has been reached in five or six months after the first symptoms were manifest.

The average duration appears to be about two years. My case terminated in about three and a half years from the time the splenic enlargement was first noticed. That duration seems to be about the longest recorded. While the first and second stages of the disease may vary and be prolonged for a period of one or more years, the cachectic stage seldom continues more than a few weeks or five or six months. Death results from progressive marasmus and intercurrent diseases. Medical treatment seems to be of no positive value in controlling the progress of the disease. Surgical treatment has arrested the process in the cases noted in the chapter on treatment. The prognosis is decidedly unfavorable without surgical intervention.

THEORY REGARDING THE ORIGIN AND NATURE OF THE DISEASE.

Although disorders of the spleen have been studied by the medical profession from the time of remote antiquity, our knowledge of the origin and nature of a number of types of disease associated with splenic enlargement is still very indefinite. Splenic pseudoleukemia shares in the general obscurity which surrounds the forms of disease closely allied to it, namely: leukemia and other varieties of the pseudoleukemia. The number of cases thus far accurately observed has been so limited that one has less than is to be desired upon which to base conclusions.

Hypertrophy of the spleen and progressive anemia are the most prominent features of the disease. The constitutional symptoms and course of the affection may be satisfactorily explained by the progressive alterations in the blood, whether other factors, aside from complications, contribute to the fatal termination, our present knowledge will not permit us to affirm or deny.

It is rational to presume that the two principal features of the disease, progressive anemia and enlargement of the spleen are either directly dependent on each other or that both are manifestations of a common cause. A study of the origin and nature of pseudoleukemia involves a consideration of the following questions: 1. Is the hypertrophy of the spleen a result of the progressive anemia and if so upon what does the anemia depend? 2. Do the chief features of the disease progressive anemia and splenic hypertrophy arise from a common cause? 3. Is the progressive anemia and general malnutrition due primarily to the pathological changes in the spleen and if so what induces those changes?

Let us first discuss whether it is probable that the splenic hypertrophy is due primarily to the alterations in the blood. (If this be true the cause

of the anemia is not apparent and the disease must be classed as an essential anemia.)

In chlorosis, the spleen is often somewhat enlarged. Chvostek examined 56 cases with especial reference to splenic enlargement in that disease. He was able to palpate the spleen in nine of the total number of cases. In primary progressive pernicious anemia the spleen may be enlarged sufficiently to be palpated. However, in both forms of essential anemia the splenic enlargement is always moderate, seldom reaching more than a finger's breadth below the costal arch. It fluctuates in size during the course of the disease and never reaches the enormous tumefaction often found in splenic pseudoleukemia. A very slight enlargement of the spleen has also been observed in secondary anemia and in anemia artificially produced, both in man and in lower animals. However, in the forms of anemia just described the spleen is often normal in size and at times atrophied. Mosler, Gast and others regard the moderate enlargement of the spleen which is present in anemia as a compensatory process. On the other hand, Immermann, Eichhorst, Müller, Neuman and others do not believe that in the conditions enumerated the spleen reverts to its embryonal blood-producing function. Others believe the enlargement due to an increased destruction of red blood corpuscles.

From all available evidence it would appear that while anemia may give rise to an enlargement of the spleen its size is always moderate and never approaches the enormous hypertrophy commonly recorded in splenic pseudoleukemia. Still greater evidence against the theory that the splenomegalia in this disease is due to anemia is afforded by the fact that in all cases thus far reported splenic hypertrophy preceded the anemia and in some cases for a period of a year. From the foregoing it is very improbable that the enlargement of the

spleen in splenic pseudoleukemia is in consequence of the progressive anemia.

The second question as to whether the chief features of the disease, progressive anemia and splenic hypertrophy arise from a common cause, is extremely difficult to discuss. It is possible that the true solution of the problem lies in that direction. However, in the absence of all direct and indirect evidence favoring that interpretation, it will not be profitable to enter into a discussion of possibilities.

On the other hand, the theory which places the enlargement of the spleen primary, and the progressive anemia secondary to the splenopathy has very much in its support. In the cases thus far reported, splenic hypertrophy has preceded the anemia and other constitutional symptoms of the disease. We must next consider whether the pathological changes which occur in the spleen are capable of inducing the profound alterations in the blood and general nutrition which accompany the disease. Accurate knowledge of the function of the spleen would be of inestimable value in the solution of the problem. Unfortunately very little is known regarding its function. An extended discussion of the various theories, regarding it is beyond the province of this paper. The following are some of the more prominent theories advocated. 1. During fetal life and shortly after birth, in man the spleen is supposed to produce red blood corpuscles. In some animals this function is retained during life. There is no positive evidence that this obtains in the adult life in man. 2. It is believed on rather unsatisfactory evidence that the spleen is engaged in the destruction of red blood corpuscles. 3. White blood corpuscles of the large mononuclear variety are probably formed in the spleen. 4. The theory of Schiff and Herzen that the spleen produced a substance (an enzyme) which being carried by the blood to the pancreas acts upon the

trypsinogen contained in the gland, converting it into trypsin, has not been confirmed by other investigators. While there is very little positive evidence as to the exact function of the spleen, it is generally conceded that the organ in some way exerts an influence on the constituents of the blood. That the spleen is not necessary to life has been demonstrated repeatedly by its entire removal. However, this does not prove that it is functionless. Various organs may perform the work of the extirpated spleen. It is interesting to note that in a few instances after removal of the organ the lymph glands have shown a moderate increase in size. Since the removal of the spleen is not incompatible with perfect health, it is not reasonable to presume that the malignant course of splenic pseudoleukemia is due to suspension of the normal function of the gland, in consequence of its hypertrophy. On the other hand, it can not be denied that the pathological changes in the spleen may alter its function in such a way as to result in grave disturbances of nutrition. If the spleen is normally engaged in the destruction of red blood corpuscles possibly an abnormally great destruction of these elements takes place as a result of splenic hyperplasia.

It is claimed by a number of investigators that the blood in the splenic vein shows a marked difference in its constituents from that contained in the splenic artery. The results obtained have varied so greatly that one is unable to draw specific conclusions. They render it very probable, however, that the normal spleen is actively engaged in metabolic processes. The complex chemical composition of the spleen and especially the presence in its tissue of a number of nitrogenous extractives such as xanthin, hypoxanthin, adenin, and uric acid strongly favors that conclusion. Aside from these substances the tissue of the spleen contains mosite, tyrosin, leucin, formic, lactic and butyric acids and

cholesterine. Its chief mineral constituent is an organic compound of iron.

Possibly chemical agents are elaborated by the diseased spleen which either in the gland or after they gain access to the circulating blood, inhibit the production of red blood corpuscles or cause their dissolution and thus induce anemia. An analogous theory explains the anemia of exophthalmic goiter on the grounds that an enlarged thyroid produces toxines capable of causing dissolution of red blood corpuscles. That a toxic substance of some nature was present in the tissue of the spleen in my case is probable from the evidence obtained by injecting the veins of rabbits with a few cubic centimeters of the filtrate of an emulsion of a small portion of the spleen. The animals died within a few hours and no adequate cause for death was present at post-mortem. Whether this toxic substance was capable of destroying the red blood corpuscles was not determined by the experiment. The blood of the rabbits showed no apparent histological changes in the several slides examined.

There is nothing in the histology of the spleen in splenic pseudoleukemia which would favor the theory that the anemia was secondary to the splenic hypertrophy. The histological changes constitute a true hyperplasia and present nothing which differentiates it essentially from other forms of splenic hypertrophy that are not accompanied by progressive anemia.

The greatest evidence, however, in favor of primary splenopathy in splenic pseudoleukemia is afforded by the results of total extirpation of the hypertrophied organ. Even after hemorrhages, edema and signs of cachexia were well developed a removal of the hypertrophied spleen has resulted in recovery. See résumé of such cases in the chapter on treatment. The complete recovery which took place after the removal of the hypertrophied spleen in five cases of splenic pseudo-

leukemia points directly to the spleen as the source of the anemia.

TREATMENT.

The treatment of splenic pseudoleukemia should be medical and surgical. The indications to be met in medicinal treatment are to build up the blood and general nutrition. Iron, arsenic and other drugs having the same therapeutic influence should be administered. Rest in bed should be enjoined and constipation, if present, relieved. Special symptoms as nausea, vomiting, diarrhea and pain require the same treatment as when due to other causes. In the later stages diarrhea may be so persistent as to require great care in its treatment. The disease is modified only temporarily by internal medication.

If the disease is primarily located in the spleen and the pernicious course of the affection is due to the effect of the pathological change in that organ upon the blood and general nutrition, it would be a rational procedure to remove the spleen as soon as the diagnosis is positive and when no special contraindication is present. The number of splenectomies performed in which this disease was undoubtedly present is very small. In reviewing the literature of splenectomy it is exceedingly difficult in many cases to determine the nature of the disease for which the operation was performed. As a rule the operator has been more concerned in the technique of his operation than with the nature of the pathological process for which it was performed. The justification of that statement is furnished by the fact that in the total number of cases, about 190, in which the spleen has been removed, a microscopic examination of the blood has been recorded in less than twenty cases and in some of these only imperfectly. Since a blood examination is necessary to the diagnosis of splenic pseudoleukemia, it would be futile to search for cases of that disease among the affections in which splenectomy

has been performed outside of the limited number of cases in which the blood has been examined.

I will give a short résumé of the cases in which splenectomy has been performed, where it seems probable that the disease present was splenic pseudoleukemia.

Case 1.—Operator, Spencer Wells. Date, 1865. Female, aged 34. Symptoms, marked anemia, slight increase in the white blood corpuscles (character of corpuscles not noted). Weight of spleen, 2672 grams. Result, death.

Case 2.—Operator, Péan. Date, 1878. Female, aged 24. Patient never had malaria nor any serious illness. Eighteen months before operation, a splenic tumor first appeared. Six months previous to operation signs of anemia present. Subsequently anemia gradually progressed. Digestion greatly disturbed, violent neuralgic pains, hemoptysis, hematemesis, hematuria and bloody stools were recorded. No leucocytosis. Weight of spleen, 1125 grams. Result: In one month patient had recovered perfectly. Subsequently died of toxic enteritis.

Case 3.—Operator, Czerny. Date, 1878. Female, aged 30. No history of malaria. Spleen, large and movable. No leucocytosis. General health very poor. Digestion disturbed. Signs of anemia. Disturbed menstruation. Weight of spleen not given. Size, 23x12x8 cm. Result, complete cure.

Case 4.—Operator, Franzolini. Date, 1881. Female, aged 22. Never in good health. At 12 years of age, suffered with edema and ascites, from which she recovered. Menstruated at 17, but always irregularly. Was subject to hysteria. Never had malaria. About two years previous to operation patient noticed constant pain in left hypochondriac region. Pain was increased on pressure and in the erect position. Patient grew weak, and when admitted to hospital a tumor was readily detected in left hypochondriac region which proved

to be an hypertrophied spleen. Sufferings of the patient and signs of anemia increased. Skin and mucous membranes very pale. Great muscular fatigue. Vomiting obstinate. Panniculus adiposus greatly reduced. Leucocytes: Five times the normal number were present. Weight of spleen, 1526 grams. Result, complete cure. All suffering ceased and the oligemia disappeared. Thirty-six days after operation the white corpuscles were reduced to one half the number at the time of the operation.

Remarks: This case was reported as a leukemia and is usually so regarded. The method employed to estimate the leucocytosis was subject to inaccuracies. An increase of leucocytes to five times the normal number is not sufficient evidence for the diagnosis of a leukemia, unless the quality of leucocytosis were that which is peculiar to leukemia. Banti is also of the opinion that this case was not a leukemia.

Case 5.—Operator, Frascani. Female, aged 16. No hereditary influence. Never had malaria or syphilis. Had noticed a large tumor in left half of abdomen for two years. During this time epistaxis, fever and diarrhœa now and then present. Mucous membranes pale. Signs of anemia began one year before the operation and were marked at time of operation. Edema and ascites present. Blood examination: red blood corpuscles, 3,900,000; white blood corpuscles, 7030 per cu. m. Hæmoglobin 68 per cent. External lymph glands slightly enlarged. Result: Death in four hours from hemorrhage. Weight of spleen, 1310 grams. Weight of liver, 1050 grams.

Case 6.—Operator, Ceci. Date, 1893. Female, aged 13. Disease began two years previous. Signs of anemia and tendency to hemorrhage from the gums. Bones normal, muscle weak, adipose tissue thin, abdominal tumor firm and smooth. Blood examination: red blood corpuscles 3,592,000, white blood corpuscles 15,000 per

cu. m. Hæmoglobin, 65 per cent. Weight of spleen, 13,000 grams. The quality of leucocytosis not recorded. Result: recovery.

Case 7.—Operator, Lindfors. Date, 1892. Female, aged 20 years. Constitution weak. Five years previous noted tumor in left side of abdomen. Signs of anemia were present. The red blood corpuscles were diminished and the hæmoglobin was especially reduced in quantity. The relation of the white to the red blood corpuscles was 1 to 250. No thyroid or lymphoid enlargements. Size of spleen, 25x15x7 cm. Result: recovery.

In all, I find seven splenectomies in which the records are sufficiently explicit to justify a very probable diagnosis of splenic pseudoleukemia. There are other cases that appear to belong to the same type of disease; but owing to the meagreness of the records I have not felt justified in including them. Five among seven cases in which one may be reasonably certain that splenic pseudoleukemia was present were cured by a removal of the hypertrophied organ—the remaining two died of hemorrhage. In not one of the seven cases, was operation performed early in the course of the disease. In at least two of the five cases that recovered the disease had advanced well into the cachectic stage. When we consider that splenic pseudoleukemia is a progressive disease, which so far as has been recorded, invariably terminates fatally when treated medicinally, it is apparent from the statistics that splenectomy should be performed as soon as the diagnosis is positive and the case not too far advanced to preclude possibility of recovery.

As a rule in splenectomy the mortality increases with the size of the spleen. In none of the cases, however, in which recovery took place was the spleen less than five times the normal size. In one case which resulted in cure, the hypertrophied organ was nearly eight times

as large as normal and the cachexia was extreme. The mortality, after operation, in this disease is very much less than when leukemia was present. Douglas records thirty-six cases of splenectomy for leukemia with only five recoveries and three of these I have included as cases of splenic pseudoleukemia.

BIBLIOGRAPHY.

Woillez: Observation d'hyp. de la rate. Union Medicale, 1856.

Guttman: Trait du diagnostic, p. 438, Paris, 1877.

Lees: A Case of Great Enlargement of the Spleen. Dublin Hosp. Gazette, 1859.

Gretzel: Ein Fall von anemia splenica. Berlin Klin. Woch., 1866.

Muller: Uber idiopathische Milztumoren. Berlin Klin. Woch., 1867.

Landouzy: Bull. de la Soc. Anat., 1873, p. 67.

Strumpell: Zur Kentniss der Anemia Splenica. Archiv der Heilkunde, 1875.

Spencer Wells: Gaz. Hebdomadaire, p. 439, 1866.

Nivet: Hypertroph de la rate. Archives generales de Med., 1832.

Hodgkin: On Some Morbid Appearances of the Absorbent Glands and Spleen. Med.-Chir. Transact., vol. xvii.

Kundrath: Zur Kentniss der Pseudoleukemia. Wiener Klin. Wochenschrift, No. 13, 1893.

Taylor: Case of Splenic Anemia or Primary Splenomegaly. Guys Hosp. Rep., iii 173, 1896.

West: Case of Splenic Anemia. Med. Chir. Transactions, 1896.

Pean: Diag. et trait. Abdom. tumeurs, 1880.

Czerny: Wiener Med. Wochenschrift, 1879.

Franzolini: L'Independ. Gaz. Med. di Torino, 1882.

Hare: Splenic Anemia. Med. and Surg. Reporter, Phila., 1897.

Debove and Bruhl: La Splenomegalie Primitiv. Bull. et Mem. Soc. Med. d'hop. de Paris, 1892.

Gaucher: De l'hypertroph. idiopath. de la rate sans leucæmia. France Med., 1892.

Banti: Dell anemia splenica Archivo della scuola d anat. pathologica. Florence, 1883.

Reudu: De la splenomegalie Primitiv. Gazz. d osp. Milano, 1894.

Banti: La splenomegalie avec cirrhosis du foie. Semaine Med., 1894.

Stein: Zur Frage der Pseudoleukemia. Weiner Med. Woch., 1897.

King: Case Splenic Anemia. Trans. Mich. Med. Soc., Grand Rapids, 1897.

Virchow: Weisses Blut Frorieps N. Notizen, 1845.

Neumann: Ein Fall von Leukemia mit Erkrankung des Knokenmarks. Archiv. der Heilkunde, 1870.

Eichhorst: Handbuch der Pathologie und Therapie.

Delbet: Production d'un lymphadenome ganglionnaire generalise chez un chien. Compt. rend. d'Acad. de Science, 1895, No. 24.

Choostek: Wiener Klin. Woch., 1893.

Banti: Splenomegalie Mit Libercirrhosis. Ziegler's Beitrage, Band xxiv, Heft 1.

Williamson: Case of Anemia with great enlargement of the spleen (splenic anemia).

THE SKIN.

A CASE OF BLASTOMYCETIC DERMATITIS.

H. GIDEON WELLS.

In the first volume of the *Johns Hopkins Hospital Reports* there is reported by T. C. Gilchrist a case of dermatitis resembling clinically skin tuberculosis, but apparently due to the presence in the lesion of a form of blastomyces. At the last meeting of the American Dermatological Association he reported a second case, in which he found a similar lesion due to the same kind of organisms. So far these two cases stand alone among the numerous blastomycetic infections, being entirely different from all other forms described by Busse and other observers.

The case to be described adds a third to this group, and its discovery so soon after Gilchrist's first report appeared makes it seem probable that a hitherto unrecognized cause of skin lesions will be found to prevail in many cases ordinarily diagnosticated as lupus vulgaris. It was presented in the clinic of Professor Senn at Rush Medical College, during my service as pathologist to the surgical clinic, and I am indebted to him for the opportunity of presenting this case.

The patient was brought to the clinic by Dr. J. T. Phillips, of West Union, Iowa, on March 23, 1897. Dr. Phillips had observed the case for over a year, and furnishes the following history. The patient is a well nourished man, 40 years of age, a native of Iowa, farmer by occupation. He presents a good personal and family history, married, has five healthy children, none of whom have ever had any similar affection, nor has any

person of his acquaintance. A thorough physical examination shows him to be free from any pulmonary or glandular involvement. The disease began eleven years ago as a small pimple on the back of the first phalanx of the left little finger. This pimple became an ulcer, which gradually enlarged, extending up over the knuckle on to the back of the hand, over which it slowly spread. It never invaded the palm. The highest it ever reached was just above the head of the radius. It extended from the junction of the palm and dorsum of the hand on the ulnar side to the base of the thumb, and grew down to the second phalanx of the index finger, to the middle of the second phalanx of the second finger, just beyond the first phalanx of the ring finger, and never extended below its starting point on the little finger. During its progress the older portions of the lesion would sometimes heal up, leaving a poor substitute for skin, which was of low resisting power, for it would repeatedly become reinvaded by the disease.

In appearance it was a raised fungating mass, in some places three-quarters of an inch above the normal level of the skin. When washed it was of a dark cherry-red color, sprinkled with cheesy pinhead-sized masses. After being left for a time the surface would become covered with a crust of pus, scales, and *debris*, which was readily removed. Secondary infection frequently occurred, sometimes producing large-sized abscesses. When the wet dressings that had been applied for some time were removed, the growth had a honeycombed appearance and bled very easily. Every ordinary form of antiseptic treatment, hot fomentations, etc., were tried, but the only evident effect was on the secondary infection. Early in its course attempts had been made at its removal by caustics, plasters, etc., without result.

Pain was constant in the hand, often especially severe at night, but the patient was able to do his farm work and felt perfectly well otherwise during all this

time. Although there were abundant opportunities for infection of other parts of the body, no other foci ever appeared, and the growth was solely by extension. Dr. Phillips considered it a case of skin tuberculosis, and Professor Senn agreed to the diagnosis. He removed the entire area involved, covering the surface by a plastic operation, with excellent results. Since his discharge from the hospital the patient has been perfectly well, and there have been no recurrences.

Cultures were made on blood serum, agar-agar, bouillon, and gelatin by rubbing small fragments over or in the media, so that any deeply located organs might be implanted. A rank growth was obtained in all the tubes, from which were isolated the *Staphylococcus pyogenes aurcus* and *albus,* and three varieties of bacilli, none of which produced any reaction when inoculated into rabbits, being evidently saprophytic putrefactive organisms. In none of the original cultures could be found any of the budding fungi to be described later.

A piece of the tissue was implanted subcutaneously into a young rabbit. In a week an abscess developed, reaching the size of a hickory nut, and on the ninth day it broke down, forming later an ulcer, with raised margins from which could be squeezed a whitish pus. A second rabbit was inoculated with this pus and had a swelling of the size of a hazelnut, which subsided and healed. The general health of the rabbits remained good, and at the end of three months the one first inoculated was killed. No lesion could be found in any of the viscera. The pus from the abscess was carefully and repeatedly examined, stained, unstained, and treated with caustic potash, but the yeast fungi could never be found. Cultures from the abscess yielded the *Staphylococcus pyogenes aureus.* The tissue was hardened in various fluids, and from this material the case has been studied.

Microscopical Examination.—The most marked

change is the great increase in the epithelial layer of the skin. Columns of epithelium are seen growing into the corium to a depth of about four millimeters, uniting masses of deeply situated epithelial cells to the superficial layers and to each other, almost exactly as it is seen in skin carcinoma. None of the appendages of the skin are present in any form. The papillæ, however, come up to within the usual distance of the surface in many places, but they can not often be traced directly down to the deeper layers of the corium on account of intervening epithelial tissue. In serial sections it is found that the papillæ are in many instances long fingerlike columns of tissue, often bending and running at right angles to the surface. These appearances can best be explained by considering the hypertrophy of the epithelium to have occurred chiefly in the deeper layers of the interpapillary processes, crowding down into the corium and distorting the papillæ by irregular expansions in lateral directions so that sections at right angles to the surface show them mostly in transverse and oblique section.

The stratum corneum is much thickened, and in many places desquamated. On its surface is scattered much *debris,* consisting of blood-corpuscles, shreds of corneum, swollen squamous epithelial cells, and many varieties of bacteria. Frequently it is found split into layers or lifted from the deeper layers by an exudate containing similar substances. The blastomycetes were never found in this *debris.* The stratum granulosum and stratum lucidum are not demonstrable.

The hypertrophied Malpighian layer, which forms the masses of epithelium existing below the ordinary level, is distinctly separated from the corium by the usual layer of cylindrical epithelial cells which appear quite normal. The prickle cells show their processes very distinctly. In the central part of the larger columns the nuclei are not numerous and stain poorly, be-

ing separated by a small space from the cell protoplasm. The cells are also separated from each other by similar spaces in many cases, giving the whole structure an œdematous appearance. Small epithelial whirls are abundant. Many leucocytes are found in the spaces between the cells, and miliary abscesses are numerous in the epithelial masses.

These abscesses can generally be found to contain one or more parasites if they be examined by serial section, and can be traced from the very earliest stages. They first show about the parasite a few swollen epithelial cells separated by a small amount of exudate containing leucocytes, which can be seen making their way between the epithelial cells toward the abscess. The abscesses appear to increase in size rather by accumulation of leucocytes than by destruction of the epithelium, for the larger ones consist of a mass of leucocytes, mostly of the polymorphonuclear variety, surrounded by layers of epithelium much flattened by pressure, and epithelial cells are found free in the contents of but a few of these abscesses. It is an interesting fact that in some of the abscesses isolated in the epithelium, and in no communication with the corium, typical giant cells are found, which must have been formed from either the epithelium or from the cells that have wandered in.

In the corium is a great increase in the cells, the nuclei of which are large and stain intensely. These cells are gathered into masses, in many places resembling granulation tissue. Polymorphonuclear leucocytes are everywhere present. Where the embryonal cells are less numerous the connective tissue is made up of cells with long anastomosing processes, resembling cells of myxomatous tissue, and containing in their meshes eosin-staining granular material and many leucocytes. The subcutaneous connective tissue contains foci of granulation tissue, and appears to be œdematous. Blood-vessels are numerous and generally dilated.

Giant cells are very numerous in the corium, often in groups of three and four, and most numerous in the deeply cellular portions. Like the giant cells of the miliary abscesses, they are identical in structure with the typical giant cell of tuberculosis, consisting of a peripheral layer of nuclei and a central mass of finely granular eosin-staining material. Vacuoles, usually larger than a nucleus, sometimes involving half the central portion, are numerous. They may be due to shrinkage, but they are equally evident in all specimens, no matter in what fluids they may have been hardened. There are, however, none of the characteristic zones of tubercular foci about the giant cells, which are scattered about with no apparent relation to the structure of the tissue in which they lie. Many sections were stained in search of tubercle bacilli, but none were found. This negative result is borne out by the results of the inoculation into rabbits.

The parasites are found chiefly in the miliary abscesses both of the corium and of the epithelium; also in the giant cells, whether loose in the corium or in the abscesses; and often they are found free in the corium, but never without more or less evidences of inflammatory reaction about them. They have never been found included in any of the tissue or wandering cells. In size the adult forms are about the size of or a little larger than a white blood-corpuscle.

In structure they are seen to be composed of four chief parts, from without inward, being: 1. A capsule. 2. A transparent zone. 3. A central protoplasmic portion. 4. A vacuole within the protoplasm.

The capsule appears under the microscope as a well-defined dark line about the fungus. The transparent zone separates the capsule from the protoplasmic center of the parasite. It varies much in thickness, sometimes being difficult to detect and again being equal to a fifth or a sixth of the diameter of the entire organism. The

protoplasm is very granular, and stains fairly well with methylene blue or iron hæmatoxylin, but not by Gram's method nor red by Gabbet's method. The vacuole is not always present, particularly in organisms that are budding or have just been separated from the parent plant, yet it probably has no relation to the process of division, for in some cases the vacuole itself seems to enter the bud and be divided off with the protoplasm. The vacuoles are located centrally, for protoplasm granules can always be found above them by focusing. Sometimes they are multiple or consist of two or three connecting lobes.

What may be considered the mature organisms, the large solitary forms, are spherical in outline, and the four constituent portions are arranged exactly concentrically. The process of division occurs in the following manner: A small process of protoplasm appears, which pushes before it the capsule and the transparent zone, making it possible that this zone consists of some firm substance rather than merely a fluid, separating capsule from protoplasm. After the protoplasm has passed a short distance beyond the original margin of the capsule the process begins to enlarge at the extremity, and a small oval bud is formed. After this bud becomes from a half to three quarters as large as the parent the capsule sends a septum across its base, shutting it off. Frequently the parent begins to bud anew before the first formed bud has become separated, and in this way a string of four to six organisms may be formed.

It can not be said that the giant cells produce any effect on the parasites they contain. Organisms in all stages of multiplication are found within them. Frequently they are found to contain what appears to be the capsule of one or more parasites, having no protoplasmic contents; but similar forms may be found in the tissues outside the giant cells, and so there is no evi-

dence that the giant cells are responsible for the changes. Neither is there anything pointing to the leucocytes as having produced any changes in the parasites.

If this case is compared with the one first reported by Gilchrist, their identity will be apparent. With Gilchrist's first report there is no clinical history or description of the lesion, beyond that it resembled a typical case of scrofuloderma. The second case is more complete in this respect. Here the history is, briefly, that the lesion had existed for eleven years and a half, starting as a pimple behind the left ear, and leaving, in its track over the face, healed scars. In its chronicity, origin, and course it resembles the case just described, but differs in that there were secondary infections on the hand, scrotum, thigh, and back of the neck, which exhibited a tendency to spontaneous healing. The case resembled lupus vulgaris. There was no adenopathy. The microscopic study showed this case to be identical with the one first described.

However, in this second case Gilchrist was able to secure the parasites in pure culture. They grew on the ordinary media, particularly on potato, and developed a mycelium stage which was never observed in the tisssues. They did not produce fermentation of lactose, glucose, or saccharose. They were pathogenic to guinea-pigs, dogs, sheep, and horses, but not to mice, and in one case not to rabbits. The failure to obtain cultures from the case under consideration may possibly be due to the presence of such a multitude of saprophytes and pus microbes, their more rapid growth having prevented the multiplication of the blastomyces. That no effects were obtained by inoculation into rabbits may be explained on the same ground, or it may have been due to a lack of susceptibility of the animal, as shown by Gilchrist's inoulation experiments.

These three cases are quite different from the well-

known case described by Busse,[1] in that in the latter the skin lesions were but part of a general infection, starting as an abscess in the tibia and producing a pyæmia. The organisms were also different, possessing nuclei staining deeply by Gram's method and other common stains, and resembling tissue cells.

The discovery of two cases of blastomycetic dermatitis so soon after the appearance of Gilchrist's complete report in the *Johns Hopkins Hospital Reports* makes it probable that this form of infection will be found to be more prevalent than at first supposed. Probably until now these cases have been passing among practitioners unchallenged as lupus vulgaris, although careful re-examination of a number of specimens removed in the surgical clinics of Rush Medical College during the past two years has failed to show any evidences of blastomyces. At present, with but two cases reported fully as to their clinical history and appearances, it is impossible to draw any comparisons that will enable the physician to tell from the clinical aspect whether the lesion is due to the tubercle bacillus or to the blastomyces of Gilchrist; the microscope alone can be relied upon to establish the difference.

October 11, 1897.

A CASE OF BLASTOMYCETIC DERMATITIS—CLINICALLY AND HISTOLOGICALLY, AN EPITHELIOMA.

W. E. COATES.

No subject at the present time is awakening more interest among pathologists than the presence of blastomycetes or yeast-like fungi in cases of dermatitis, carcinoma

[1] Ueber Saccharomycosis hominis. Virchow's Archiv., Bd. cxl, heft 1.

and sarcoma. The case reported tonight can be added to the cases of blastomycetic infection previously reported in the United States by Gilchrist,[1] Gilchrist and Stokes,[2] Wells,[3] Hessler,[4] and the two cases recorded in an article by Hyde, Hektoen and Bevan,[5] making a total of seven cases already reported.

In keeping with the cases so far reported I have called the case one of blastomycetic dermatitis, although from the clinical and histological features of the growth it would be justifiable to call it a case of blastomycetic epithelioma.

The brief and rather imperfect history of the case is as follows:

Mr. J. F. F., Irish American, 37 years of age, by occupation a stationary engineer, presented himself for treatment at Dr. Harsha's clinic at the College of Physicians and Surgeons of this city, about May 15, 1898. The patient was suffering from a growth on the lower lip, the growth being situated at the junction of the mucous and dermal surfaces, involving about the middle third of the lip.

The patient's general appearance was good, he seemed healthy and well nourished, there was no history of syphilis or tuberculosis, but a history of a previous operation for the removal of a similar growth from the outer margin of the right lower eye-lid, was obtained from the patient.

This growth from the eye-lid had been removed several weeks before patient presented himself at Dr. Harsha's clinic, by Dr. William A. Fisher at the dispensary clinic of the Chicago Eye, Ear, Nose and Throat College. The scar resulting from Dr. Fisher's operation had healed kindly at the time the patient was first seen by Dr. Harsha.

From the appearance of the growth on the lip, together with the previous history, Dr. Harsha made a diagnosis of epithelioma and removed the growth. The operation was a success, the wound healing by first intention within one or two weeks, after which time no further history of the case could be obtained. Unfortunately, neither the records of the Eye, Ear, Nose and Throat College nor of the College of Physicians and Surgeons throw any light on the duration of the growths on the right eye-lid and on the lower lip, nor is it stated which growth was primary.

The brief record of the case from the Eye, Ear, Nose and Throat College states that the patient had a growth on the

outer margin of the right lower eyelid, also one on the lower lip, and that the glands at the angle of the jaw on the right side were enlarged. Dr. Fisher removed the growth on the eye-lid and referred the patient to Dr. Harsha's clinic at the College of Physicians and Surgeons for treatment of the lip and the enlarged glands.

Dr. Fisher's diagnosis, based on the clinical history and the microscopical examination of the growth on the eye-lid made by the Columbus Medical Laboratory was multiple epithelioma.

The growth removed by Dr. Harsha was sent to the Clinical Laboratory of the College of Physicians and Surgeons for microscopical examination, which was made by one of my students, now Dr. Fred G. Harris.

The clinical diagnosis of epithelioma was verified at that time by the microscopical examination, although the presence of a few isolated giant cells in the sections raised the question as to the possibility of the growth being tubercular in origin, or possibly a mixed tuberculosis and epithelioma. But Dr. Hektoen having called my attention to the presence of blastomycetes in some of my slides from a similar case from Dr. J. B. Murphy's clinic, I corroborated his findings in Dr. Murphy's case and later demonstated the presence of numerous blastomycetes in the growth removed by Dr. Harsha.

Before taking up the pathological findings in Dr. Harsha's case, I would call attention to certain points of difference in the clinical history of this case and the cases reported by Gilchrist, Gilchrist and Stokes, Wells, Hessler, and Hektoen in America, and Busse.[6]

In the cases reported by the above, with the exception of Hessler's case, there was a much larger area of epithelial surface involved than in this case; in fact, there was more or less of a diffuse dermatitis.

Busse's case was one in which the skin lesions were part of a general systemic infection, starting as an abscess in the tibia and producing a pyaemia. The organisms in Busse's case also differed, possessed nuclei, stained deeply by Gram's method and other common stains, and resembled tissue cells.

In Hessler's case, the lesion appeared as a pustule—was diagnosed as a pustule, and no mention is made of any histological findings. Possibly, had we a better history of the patient in this case, the clinical history would

be found to agree better with the cases previously reported. With the history obtainable, the growth on the eye-lid, the growth on the lip at the point where the lip was constantly irritated by the use of a corn-cob pipe (suggestive of a similar irritation by a pipe in smoker's cancer), the enlargement of the glands at the angle of the jaw on the affected side, the clinical appearance of the two growths and the clinical diagnosis as given by several clinicians—all these facts point to the possibility and probability of the growth being an epithelioma with the blastomycetes present as a probable cause If not an epithelioma, then we have to deal with a type of growth that undoubtedly has been repeatedly mistaken by able clinicians and pathologists for epithelioma.

Description of the specimen:

As previously stated, the growth occupied the middle third of the lower lip, consisting of a raised nodular mass about the size of a hazel-nut. The specimen was fixed and hardened in formalin and alcohol (formalin 5 parts, alcohol 100 parts), imbedded in paraffin, stained with haematoxylin and eosin, methyl blue, carbol fuchsin and methyl blue, etc.

By careful searching the blastomycetes could be readily detected in the sections stained with haematoxylin and eosin, especially where the sections were decolorized in 1½ per cent. hydrochloric acid alcohol after staining in haematoxylin, then passed through distilled water, saturated solution of lithium carbonate, distilled water, and weakly counter-stained with watery eosin.

Single staining with the anilin dyes such as methyl or methylene blue, fuchsin, carbol fuchsin, etc., gave good results when the stains were diluted to about half the strength used for ordinary bacteriological staining. But by far the best sections were obtained by staining in carbol-fuchsin at 45 C. for thirty minutes, decolorizing to a pink color in Ebner's solution, washing in water, counter-staining in dilute methyl or methylene blue for five or ten minutes, dehydrating by passing through several changes of alcohol, and clearing in oil of cloves. Sections so treated will show muscle and connective tissue fibers stained pink or red, epithelial cells, nuclei, leucocytes and blastomycetes stained blue.

The use of Ebner's solution seems to act as a mordant, or in some manner effect the staining qualities of the blastomycetes, as they appear to better advantage in the method de-

scribed than where the ordinary simpler methods are used.

The objection to haematoxylin lies in the fact that the blastomycetes are either very faintly stained or else take no stain at all.

The sections include the elevated nodular mass and the underlying tissue, also a portion of normal skin from the lip on one side of the nodule, and a portion of normal mucous surface on the other side, so that it has been possible to trace the disease process through practically every step from the normal to the abnormal.

Histologically, the growth as shown in a large number of sections may be described as an epithelioma containing in some places focal accumulations of leucocytes, cell débris, etc., constituting miliary abscesses.

The blastomycetes are found in many of these miliary abscesses, the number of parasites ranging from one to half a dozen in a section of an abscess cavity, their absence in some of the cavities being due to the fact that that particular portion of the abscess did not contain any. Careful estimation of the number of parasites present in a given miliary abscess by means of serial sections would probably show that several dozen or more were present

These organisms correspond in size, shape and process of budding and division, location in the tissues, staining properties, etc., with the blastomycetes described in cases of dermatitis by Gilchrist and Stokes, Wells and Hektoen in the United States; and by Sanfelice, Roncali, Kahane and other European investigators as present in neoplastic growths in man and animals. The parasite present in this case occurs as a round or oval highly refractive, doubly contoured organism possessing a distinct capsule from which the finely granular and usually vacuolated protoplasm is separated by a clear zone.

The mature forms have an average diameter of 12 mikrons. They occur singly, in pairs, in irregular groups of from three to six, occasionally in short chains consisting of four or five oval or slightly rectangular bodies. Some of these "chains" resemble hyphæ or the

beginning of a short mycelium. The most common forms are the isolated round bodies, and equally numerous are the budding forms consisting of a single round or oval cell from which a single bud is given off.

That these organisms have a direct bearing on the pathological changes present in the tissues cannot be questioned after a careful study of a large number of sections—the relation between cause and effect is too apparent to admit of any doubt.

As previously stated, the tumor nodule as seen in the sections contains normal skin epithelium and also normal mucous epithelium, placed one on each side of the nodule. The study of the sections should begin at the border zone between the normal and abnormal tissue in order to appreciate the distribution of the parasites and their relation to the changes caused by their presence. These changes may be summarized as follows:

1. The blastomyces penetrates the stratum corneum, stratum lucidum, and stratum granulosum by working its way through the intercellular spaces, or possibly through some defect of the superficial epithelium, until it finally reaches the Malpighian layer, which seems to be the natural abiding place of the parasite.

Careful search fails to find the blastomycetes in the perfectly normal epithelium of the sections—where the parasite is found, are found evidences of tissue change.

It has been found in some of the sections between the cells of the corneum and granular layer, also in the débris made of blood corpuscles, shreds of degenerated corneum, etc., scattered over the surface of the corneum proper at the margins of the diseased area.

Wells states that in his case the blastomycetes were never found in this débris.

2. The parasite having reached its seat of activity—the Malpighian layer—begins to produce itself by a process of budding, possibly by the development of mycelium, and probably by spare formation in a manner

analogous to the parasitic fungi which cause such havoc among vegetables, plants, shrubs and trees. It is a question whether these so-called blastomycetes are not closely related to the well-known orders of parasitic fungi familiar to the vegetable biologist and agricultural pathologist.

Careful examination of the sections shows that there are numerous small round bodies present in some of the miliary abscesses that are too regular in outline and bear too definite a relation to the large doubly contoured blastomycetes to be other than different forms of the fungus. These bodies vary in size from that of a large micrococcus to that of the nuclei of polymorphonuclear leucocytes, and some, at least of these bodies, are probably spores, or smaller forms of the fungus. Occasionally round or oval yellow or yellowish brown bodies are found, which at first glance resemble masses of blood pigment, but which are possibly related to the easily recognized large form of the fungus. The resemblance of these yellow bodies to the yellow uredospores and teleutospores, spores of some species of parasitic plant fungi is worthy of more careful investigation.

3. The effect of the blastomyces on the epithelial elements is that of an irritant—the irritation resulting from the presence of the parasite as a foreign body combined with the effects produced by toxines that are undoubtedly elaborated during the process of growth.

One of the earliest effects is undoubtedly a dissolution of the intercellular cement substance of the neighboring epithelium along with more or less disintegration of some of the epithelial cells themselves. Leucocytes and lymph corpuscles are attracted to the point of irritation and there results a miliary abscess. This miliary abscess continues to increase in size with the growth of the blastomycetes and the consequent elaboration of toxines. In some of the larger abscesses are found multinuclear giant-cells of the tuberculous type,

but repeated examinations have failed to detect tubercle bacilli.

The abscesses appear to increase in size rather by the accumulation of leucocytes than by destruction of the epithelium, for the larger ones consist of a mass of leucocytes, small round bodies that are either nuclei of degenerated leucocytes or else possibly spore bodies, or both, surrounded by layers of epithelium much flattened by pressure. Some of the larger abscesses contain loosened epithelial cells mixed in with leucocytes, tissue debris, etc. Scattered through the intercellular spaces of the epithelium around the abscess cavities are to be found polymorphonuclear leucocytes.

Gilchrist and Stokes, Wells and Hektoen, mention the presence of blastomycetes within the giant-cells, but the giant-cells in this case do not seem to contain them.

4. Accompanying the formation of the miliary abscesses occurs a marked hyperplasia of the epithelium which gives to the sections the typical appearance of a squamous-celled carcinoma.

Where the blastomyces has first located, in the superficial layers, as in the stratum corneum, stratum granulosum or upper surface of the Malpighian layer, a marked hypertrophy of these upper layers occurs around the abscesses, causing the elevated and nodular appearance of the growth. Some of these superficial abscesses open through the stratum corneum, discharging their contents on the skin surface and in that way helping to spread the infection.

If the infecting organism penetrates to the interpapillary processes either by penetrating the superficial layers, or traveling by way of the lymph spaces, the result is similar—marked hyperplasia of the interpapillary epithelium in the shape of variously shaped branching downgrowths.

These polypoid branching downgrowths of epithelium penetrate the corium to a depth of several millimeters.

turning and branching in various directions. The papillæ of the corium come up to the usual distance from the surface on the borders of the tumor nodule, but in the center of the growth all trace of normal papillæ is lost, and they can not often be traced down to the deeper layers of the corium on account of the intervening epithelial tissue. The papillæ often form long finger-like columns of tissue, bending and running at right angles to the surfaces or enclosing concentrically arranged masses of epithelium in the center of which are pearly bodies so common in epithelioma.

Wells explains these appearances by considering the hypertrophy of the epithelium to have occurred chiefly in the deeper layers of the interpapillary processes, crowding down into the corium and distorting the papillæ by irregular expansions in lateral directions, so that sections at right angles to the surface show them mostly in transverse and oblique sections.

Here and there the abscess cavities in the epithelial downgrowths apparently break into and merge their contents with an area of inflammatory cell infiltration in the corium. Such areas may contain blastomycetes and also giant-cells. In these areas there seems to be a general mixing of epithelial cells, connective tissue cells, giant-cells, and inflammatory cells, all thrown together in an irregular mass, all outlines of normal structure being lost.

5. Some of the changes in the corium have just been mentioned but a more complete description is necessary. The tissue between the epithelial dowwngrowths presents acute and subacute inflammatory changes, but only a few typical miliary abscesses.

Miliary abscesses where they occur in the corium, are usually on the border line between the tissues of the corium and the hypertrophied epithelial downgrowths of the Malpighian layer; in fact, they appear to have broken into the corium proper as a result of dissolution

of continuity of tissue. Some sections contain few, if any giant-cells in the corium; others may show half a dozen or more in a single field of marked inflammatory cell infiltration.

Taking the corium as a whole we find a great increase in the normal cellular elements, these new cells are gathered into masses, in many places resembling granulation tissue. Polymorphonuclear leucocytes are present everywhere. The subcutaneous tissue, consisting of the subcutaneous fat cushion and the underlying muscular tissue, is more or less infiltrated with inflammatory cells, plasma cells, mast cells, eosinophile cells, etc. Blood vessels are numerous and are usually dilated and engorged.

In concluding the account of this case, careful consideration should be given to the following points:

1. Clinically and histologically it would be justifiable to call the growth an epithelioma—if not an epithelioma, then we have to deal with a type of growth not easily differentiated from epithelioma if we admit the possibility of carcinomatous growths being caused by pathogenic blastomycetes, as claimed by Sanfelice, Roncali, Kahane, and other European investigators.

2. If not an epithelioma, the name "Blastomycetic Dermatitis," proposed by Gilchrist, might be used to define the growth.

"Blastomycosis of the Skin," a name proposed by Buschke in 1898, might also serve the purpose. Buschke defines this affection as a primary disease of the skin due to pathogenic blastomycetes, clinically resembling carcinoma, but without its hard edges, histologically belonging to the granulation tumors, and anatomically occupying a middle ground between mycosis and infective granulation tumors.

3. Whether this growth be defined as an epithelioma or a blastomycosis, the fact remains that the blastomycetes present have acted as a determining cause in the

epithelial proliferation which forms such a marked feature of the growth.

This one fact—epithelial proliferation due to a parasitic fungus—should stimulate investigation to determine the possibility and probability of similar or closely related fungi being present in malignant neoplasms and acting in a similar manner.

4. The vital necessity of thorough and intimate cooperation between the specialist in animal pathology and the specialist in vegetable biology and pathology.

5. The need of a better and more uniform classification of fungi, together with a closer study of the parasitic forms causing diseases in vegetable tissues with a view to determine the possibility of a transference of parasitical activity from plant to animal tissue.

On Nov. 15, 1899, the patient again came under observation for the treatment of a crushing injury of the finger, and the following additional information was obtained. In January, 1898, he suffered from a very painful rheumatic condition of the knees and elbows, accompanied by little swelling, and lasting about two weeks. Following this there was severe pain in the right breast and under the right shoulder blade. This sickness confined him to bed for about three months, was accompanied by cough and bloody expectoration, and was pronounced pleuropneumonia by the attending physicians. He lost 35 pounds in weight.

While recovering from this attack, a small, hard swelling appeared on the right lower eyelid near the outer angle. This nodule softened and was repeatedly opened with a needle, but contained little pus at any time. It continued to enlarge, attaining the size and form of a bean at the time of its removal, which was about three weeks after its appearance.

One or two weeks after the appearance of the swelling on the eyelid, a similar, but softer nodule developed on the middle of the lower lip, which increased rapidly in

size, reaching the size of a hazel nut in about three weeks, when it was excised by Dr. Harsha. This excised nodule forms the subject of this paper. Soon after the growth on the lip made its appearance, a nodule developed on the posterior surface of the middle finger of the right hand, just below the base of the first phalanx. It reached a size of $\frac{1}{4}$x$\frac{5}{8}$ inch in three weeks, and was curetted out by Dr. C. C. O'Byrne, Dr. Harsha's assistant. The patient states that about the same time some eight small nodules appeared on each lower extremity, being more numerous on the anterior and external surfaces of the thighs, only one or two below the knees. They were small, the largest $\frac{3}{8}$ inch in diameter, shot like, blood-red in color, containing no pus, and after 4 or 5 weeks could be brushed off.

The patient states that the glands of the neck, behind the angle of the jaw on the right side, became enlarged about two weeks before the growths appeared on the eyelid and lip. These enlarged glands formed a mass $1\frac{1}{4}$ inches in diameter, and after persisting about a month, gradually disappeared. At present (Nov. 15, 1899) the scars from the several operations show distinctly: there are no glandular enlargements and no visible signs of nodules or tumor-like growths.

The additional history does not change the writer's opinion of the histological resemblance of the growth on the lip to squamous-celled epithelioma, but introduces some new questions. What, if any, relation is there between the attacks or rheumatism and pleuropneumonia and the enlarged glands and tumor-like nodules on the eyelid, lip, finger and lower extremities? There are two possible solutions, either of which may be tenable. The skin lesions were one of the manifestations of a general systemic blastomycetic infection; or the skin lesions resulted from local infection by blastomyces which found a fertile soil in a system weakened by rheumatism and pleuropneumonia. The writer is inclined to the view

that there was a general systemic infection by the blastomyces.

May 8, 1899.

BIBLIOGRAPHY.

1. Johns Hopkins Hospital Reports, 1896, Vol. i, p. 269.
2. Johns Hopkins Hospital Bulletin, July, 1896; Journal of Experimental Medicine, January, 1898, p. 53.
3. New York Medical Journal, March 26, 1898.
4. Indiana Medical Journal, August, 1898.
5. British Dermatological Journal, June, 1899.
6. Virchow's Archiv, 1895, Bd. cxl, H. 23.

DISCUSSION.

Dr. Hektoen.—I have recently had the good fortune to demonstrate the blastomycetes in the tuberculiform lesions upon the back of the hand in a case under the care of Drs. Hyde and Bevan. Later Mr. H. E. Davies, in my laboratory, secured the organism in pure culture. It is a non-fermenting, yeast-like organism which grows readily upon all ordinary media, but best upon wort-agar. In some media a more or less well-marked mycelium is produced. The organism is pathogenic for various animals, causing suppurative and productive lesions, some of the animals dying from marasmus.

In a second case which occurred in the clinic of Dr. Murphy, the material being placed at my disposal through the kindness of Dr. Coates, blastomycetes were also found in the lesions. In this case the lesions—an oval, raised, superficially ulcerating area—was situated on the skin of the leg.

In both cases the clinical appearance greatly resembled tuberculosis and also carcinoma. In neither was there any glandular involvement, however. The histological changes were identical with those described by Gilchrist, Wells and Dr. Coates—marked epithelial hyperplasia, readily mistaken for carcinomatous invasion, associated with cellular infiltrations and quite characteristic miliary abscesses, containing double contoured organisms, and occasional giant cells of the tuberculous type. It seems to me that we are hardly justified in speaking of the products of these infections as carcinomatous or epitheliomatous because their clinical course seems to differ from that of carcinoma.

A CASE OF MYOMA OF THE SKIN.

MAXIMILIAN HERZOG.

Myomata of the skin are quite rare. There are hardly more than a dozen cases to be found reported in the entire medical literature. Virchow[1] has reported the case of a woman 32 years old who had been suffering for a number of years from several nodular masses about the breast; these masses Virchow describes as muscular tumors. Unna[2] states that those parts of the skin which normally contain a larger amount of unstriped muscle-fibers, such as the scrotum, the labia majora, and the area around the mammilla are most liable to give rise to the occurrence of myomata. Cases exhibiting the tumor have been reported by Verneuil and Besnier,[3] Arnozan and Veillard,[4] Brigidi and Marcacci,[5] Jadassohn,[6] Hess,[7] and Lukasiewicz.[8]

These myomata may arise from one of three sources, either from the arrectores pilorum, from the vessel-walls, or from those deep strata of muscle-fibers which are found in the scrotum, the labia majora, or the region of the breast. Jadassohn and Lukasiewicz, for instance, report a case in which they traced the origin of the tumor to the arrector muscles. Hess, in his case, saw the neoplasm starting from the vessel-wall, but could not find that the arrectores took any part. This author also mentions the presence of elastic fibers and basophilic cells in his tumor.

I am able to add a case to the scanty list. Unfortunately, I could not obtain many clinical data with reference to it, and the best history obtainable is the following: There had been removed from the cheek of a man, forty-five to fifty years old, a nodule about one centimeter or less in diameter; it had been growing slowly, had been quite painful, and the skin had not been movable over it. It seemed, on the contrary, quite

firmly adherent to the tumor. There was no ulceration. The excised nodule was referred to me with the request to verify the probable clinical diagnosis of carcinoma (epithelioma) of the skin.

Pathological Anatomy.—The small tumor mainly consists of involuntary, unstriped muscle-cells or fibers. They present in their shape, nuclei, and general arrangement those features usually found in myomata, namely the formation of groups or bundles of fibers which run in various directions and interlace freely. It can be clearly demonstrated in a number of sections that the cells of the neoplasm take their origin from arrectores pilorum. The unstriped muscle-cells forming these bundles have proliferated outwardly as well as inwardly toward the epidermis as well as toward the derma.

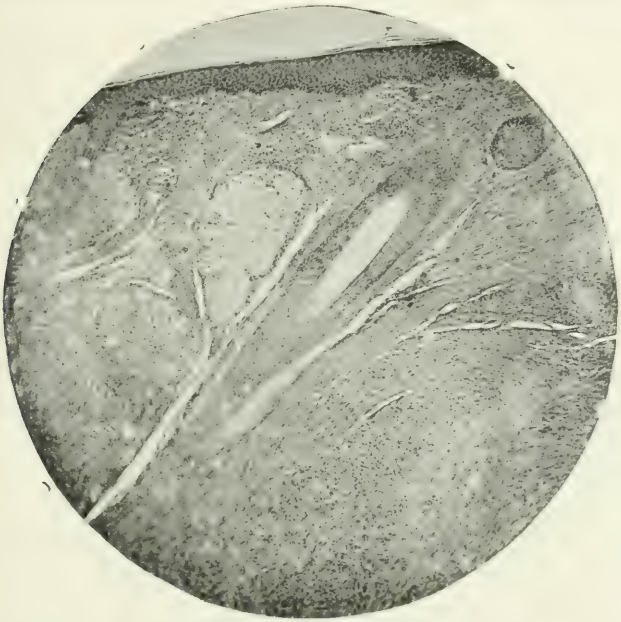


FIG. 1.—Leitz obj. No. 3; eye-piece No. 3. Section showing a hair-bulb with a sebaceous gland (to the left) and its arrector muscle (to the right), from the cells of which the neoplasm arises.

Where the epidermis overlies the neoplasm it has, in consequence of the growth of the tumor, become thinned. The epithelial strata form an even layer, there being no rete pegs. The papillæ of the derma have likewise disappeared and it may be said that the derma has become completely obliterated by the tumor tissue. The bulk of the latter, as already stated, consists of very typical

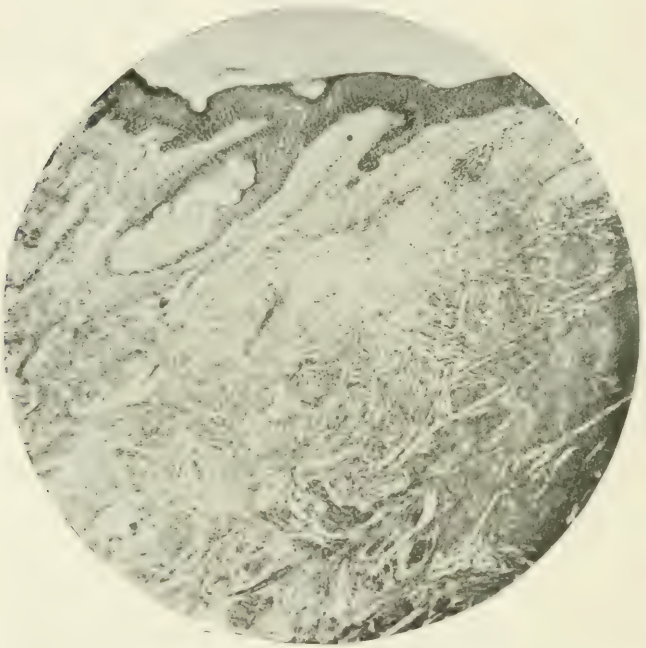


FIG. 2.—Magnification as above. Section from near outer margin of tumor, showing network of interlacing bundles of fibers and broad bands of elastic fibers.

unstriped muscle cells, but besides these, there are found in some places areas of dense round-cell infiltration. The round cells are of the type of small mononuclear lymphocytes. There are also found in these conglomerations of small mononuclear lymphocytes some basophilic leucocytes ("Mastzellen"). These cells, which could be very nicely demonstrated with the Ehrlich-

Westphal carmine-dahlia stain are also found here and there between the tumor cells proper. Elements forming the tumor also comprise elastic fibers. It is usually said that all myomata contain quite an amount of elastic tissue; however, this statement is not quite correct. It seems that the amount of elastic tissue found in myomata varies a good deal, and I have recently, for in-

FIG. 3.—Leitz pantachr. 7 mm.; eye-piece No. 3. Section showing an area of dense small round-cell infiltration.

stance, examined a large myoma of the ovary where I failed to demonstrate any elastic fibers at all. I mention this here because it appears that myomata vary a good deal with reference to the presence of elastic fibers according to their place of origin.

The myoma of the skin here described was found to be especially rich in elastic fibers, particularly those places where parts of the derma were still preserved. It is evident that the elastic fibers found in the substance of the

tumor were derived from the derma, which is so rich in these elements.

The methods used to exhibit the elastic fibers in the tumor substance, where they form to a certain extent sheaths around the muscle-bundles, into which they also penetrate, were the Mallory-Ribbert, and the Weigert[9] stain. The latter method has been published quite recently, and it may, therefore, be desirable to describe it here.

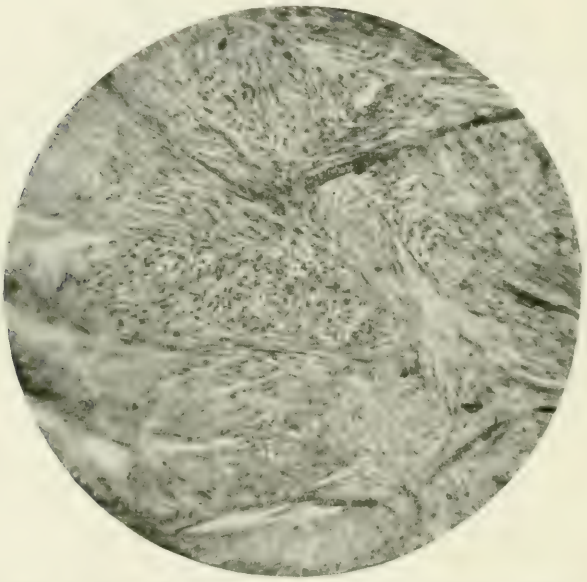


FIG. 4. Magnification as above. Section stained according to Mallory-Ribbert to demonstrate elastic fibers.

One (1) gram of fuchsin and two (2) grams of resorcin are dissolved in 200 c.c. of water by boiling in an evaporating dish. When boiling add 25 c.c. of liquor ferri sesquichlorid; stir and keep on boiling for two or three minutes; cool and filter. Dry residue in evaporating dish and add filter which has likewise been dried. Add 200 c.c., 94 per cent. alcohol and boil while stirring. When cold add enough alcohol to bring the whole

again to 200 c.c.; add 4 c.c. HCl. The stain is now ready to be used as follows:

1. Stain sections for twenty minutes to one hour.
2. Wash in 95 per cent. alcohol, lift stained section on slide, and dry with filter-paper.
3. Clarify with xylol (carbol-xylol or oil of cloves must not be used).
4. Mount in Canada balsam dissolved in xylol.

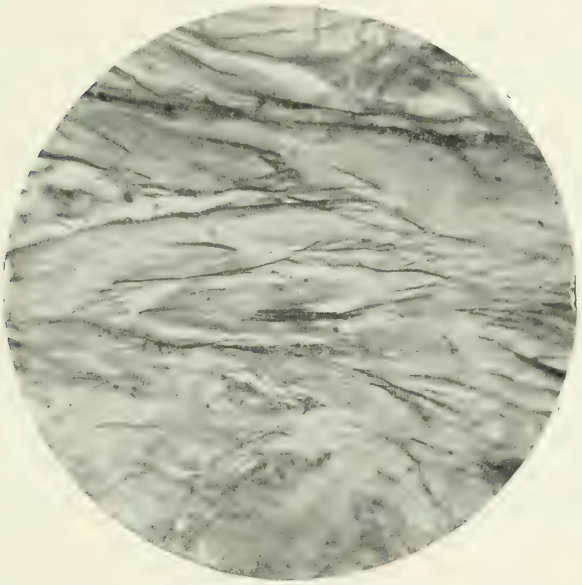


FIG. 5.—Magnification as above. Section stained according to Weigert's method to demonstrate elastic fibers.

The method as stated furnished excellent results. The elastic fibers occurring in the myoma under discussion stand out very sharply, the color being a deep blue-black. Even the finest fibers can be distinctly seen so that one gets a picture reminding one of a bare branch with twigs from which the leaves have dropped off.

These neoplasms are by no means entirely harmless from a clinical point of view. If occurring on the face

or on other exposed parts of the body they are objectionable from purely cosmetic reasons, but besides this, they are, as a rule, quite painful, as was the little tumor in our case. They are, as a rule, multiple, and they have a tendency to recur after removal, sometimes for years. They may not recur exactly at the same spot from which they have been removed, but they do appear in new crops at other points, and in some of the cases reported patients have for years been suffering from the attendant pain. It is probable that this pain is caused by pressure upon the peripheral sensory nerves so richly developed in the skin.

May 9, 1898.

BIBLIOGRAPHY.

1. Virchow: "Ueber cavernoese Geschwuelste," etc., Virchow's Archiv, vol. vi, p. 553, 1854.
2. Unna: "Die Histopathologie der Hautkrankheiten," Berlin, p. 863, 1894.
3. Verneuil, Besnier: "Les Dermatomyomes," Annales de Dermatologie, p. 25, 1880, and p. 321, 1885.
4. Arnozan and Veillard: "Myomes de la peau," Journ. de Med. Bordeaux, 1881.
5. Brigidi and Marcacci: "Des myomes cutanes," Annales de Dermat., 1882.
6. Jadassohn: "Multiple Myome der Haut," Virchow's Archiv, vol. cxxi, p. 88, 1890.
7. Hess: "Ein Fall von multiplen Dermatomyomen an der Nase," Virchow's Archiv, vol. cxx, p. 321.
8. Lukasiewicz: "Ueber multiple Dermatomyome Auspitz," Archiv f. Dermatol. u. Syphil., vol. xxiv, p. 33, 1892.
9. Weigert: Centralblatt f. Allgem. Pathologie, etc., May number, 1898.

A CASE OF PAGET'S DISEASE (MALIGNANT PAPILLARY DERMATITIS).

MAXIMILIAN HERZOG.

In 1874 Sir James Paget described a disease of the skin of the female mammary gland which was then looked upon as a chronic eczema leading finally to a carcinomatous degeneration or process. Later on other observers, particularly French and German authors,

came to the conclusion that Paget's disease even at the early stage is not to be looked upon as a chronic eczema at all. Such French writers as Darier and Wickham, who first called attention to the cellular inclusions found in Paget's disease, in the proliferating epidermal cells, were of the opinion that the affection is one "sui generis" depending upon specific coccidia. This view, however, has been again almost entirely abandoned, and the disease is now generally looked upon as a peculiar, very slowly progressing form of carcinoma. This view is now, for instance, held by Karg, Unna, Ziegler, and English and American writers who have had a chance to observe cases of this rare affection. A case of Paget's disease was some time ago reported in our country by Wiggins and Fordyce[1], who have illustrated their description by excellent cuts.

Darier himself in a monograph published in Besnier and Fournier's "Iconographie des Maladies Cutanés, etc. (Paris, 1898, p. 247), while he still mentions his former views with reference to the coccidial nature of the cellular inclusions, has apparently with resignation abandoned his earlier opinion, because he says: "En raison de leur apparence si differente de celle des cellules malpighiennes au millieu desquelles ils sont disséminés, J'ai cru pouvoir considerer ces elements comme des parasites, comme des coccidies. Cette opinion aussi defendue par Wickham et d'autre n'a pas prevalu."

According to Darier the disease has been rarely observed before the 30th year, as a rule after the 45th year of life. The majority of patients have given birth to children and nursed them. There are, however, on record three cases of Paget's disease occurring in men. In one of these three cases the seat of the affection was the usual one, in two cases the scrotum and the perineum were affected. Darier now holds that Paget's disease is of the nature of a carcinoma, characterized however by

1. New York Medical Journal. 1897.

the following particular clinical features: First, remarkably slow development, especially during the earlier stages. Second, a minor degree of malignancy shown by the fact that recurrence after removal is slow. Third, involvement of the axillary and other neighboring lymph glands being absent for a long time, and only occurring towards the very last.

It is not necessary to refer, in these short introductory remarks, to the histology of Paget's disease, as reported by others, since the case to be reported offers in its main features a typical picture of the microscopic pathology as usually described.

The case occurred in the practice of Dr. Weller Van Hook, to whom I am indebted for the following short abstract of the history:

Mrs. X., 40 years of age, had three children, the youngest one of which is 11 years old. About three months before Dr. Van Hook saw her she had a small elevation, situated about ½ inch above the right nipple. There was no pain, itching or other evidence of sensory disturbance until 10 weeks ago, when patient accidentally injured the little mass with a string. Some hemorrhage occurred, and the mass remained vividly red, looking like granulation tissue. Dr. Van Hook some time in February, 1899, removed, at the Policlinic Hospital, the little mass, and it was referred to me for examination.

The small piece of tissue excised when first examined was found to be soft and oedematous, its upper surface pinkish or rose red, the lower even and moist. It was fixed in Zenker's fluid, embedded in paraffin; sectioned and stained according to various methods, including Unna's polychrome, methylene blue, orcein stain.

The microscopic examination shows that both the epidermis as well as the derma are materially thickened, the former by a proliferation and extensive increase of epithelial cells, the latter by an enormous infiltration with round cells of various types, to be more fully described below. These cells infiltrate the papillary layer, the derma proper, and following the course of the vessels they descend into the cutis. Wherever these infiltrating

round cells are found, they have pushed apart the fibrous connective tissue. In the epidermis we find the stratum germinativum thickened, its cells are large, they do not show any prickles. The nuclei are large and vesicular and as a rule poor in chromatin, the nucleoli large and deeply stained; a few karyokinetic figures were found in the innermost layer of the stratum Malpighii. The rete pegs in some places penetrate deeply into the derma and even into the cutis; in other places they have by extensive cell proliferation become so thick and wide that there is practically no dermal papillary layer left. In still other places there are found isolated epithelial nests in the derma, surrounded everywhere by connective tissue elements. The epithelial cells of the stratum germinativum show a tendency to become vacuolated, so that the nucleus is found in a space from which the cell protoplasm has retracted. Some of the cells contain those deeply staining inclusions which were looked upon by Darier, Wickham and others as coccidia. These elements are however now generally considered not to be protozoa. In our case it can in some sections be clearly seen that these inclusions are leucocytes which have wandered from dermal vessels into the epidermis and are here found either between or inside of epithelial cells. When they are found in the latter position they are surrounded by a vacuole. Karg in his often quoted article on "Carcinoma," (*Deutsch. Ztschr. Chir., Vol. 34.*) describes a case of Paget's disease and takes the inclusions in the epithelia to be leucocytes. He looks upon the latter as elements destined for the nutrition of the epithelial cells. Whatever may under certain conditions be the function of migrated leucocytes, in a case like the present one, a type of carcinoma, the leucocytes found in and among epithelia, appear to have quite a different function. I think that they are primarily attracted by chemotactic influences in order to exert a protecting phagocytic or germicidal action. Whether they are al-

ways equal to this task or whether instead of destroying they are destroyed themselves is of course another question.

Next to the stratum germinativum we find a stratum granulosum, the cells of which are densely filled with keratohyalin, but the epithelial cells containing this substance do not pass into the typical state of cornification. The keratohyalin granules, it appears, are discharged out of the cell body and are then found lying between the cells. The latter themselves become homogeneous hyaline spheres of very large size; they are evidently oedematous and in a condition of hydropic swelling. These spherical bodies seem to be surrounded by a somewhat condensed tissue, a kind of membrane which is probably of a cornified character, since it stains violet with Gram's stain. In the derma the connective tissue fibers are pushed apart by a dense round cell infiltration. In our case, like that described by Unna, (*Histo Pathol. I. Hautkrkh.*) the infiltration in the papillary body, derma and cutis consists in its great bulk of plasma cells and among these are plasma-mast cells with their dense coarse granulations; there are also found some polymorphonuclear leucocytes, lymphocytes and transitory forms between the latter and plasma cells. Besides these cells are seen a very large number of eosinophilic cells in the inflammatory area. So great is their number that I first mistrusted the correctness of the impression, but sections stained with eosin solutions (watery and glycerin solutions) exclusively, showed that there could be no error as to the observation.

The cell infiltration is always densest around the vessels and the vessel walls themselves frequently show infiltration with various cells, including plasma and eosinophilic cells. In the smaller vessels the enormous increase of leucocytes above the normal is very striking. Among the white cells found in the vessels are polymorphonuclear leucocytes, mastcells, lymphocytes and

forms intermediate between the latter and plasma cell and eosinophilic leucocytes. These cells frequently are found clinging to the inner side of the vessel wall; occasionally one sees a cell migrating through the wall and among these also plasma cells and eosinophilic cells.

In one of the most recent contributions about plasma cells by Krompecher,[2] the author, who has been engaged in the study of these cells for three years, states that he has never seen a plasma cell with a karyokinetic figure. It must of necessity be a matter of great difficulty to recognize and identify a cell undergoing mitosis as a plasma cell. Plasma cells are generally characterized by an excentric position of the nucleus which as a rule is comparatively poor in chromatin. The latter is distributed peripherally, next to the nuclear membrane, and the whole nucleus is often surrounded by a light ring or halo. The cell protoplasm is quite abundant and stains markedly with the basic aniline stains. The cell body as a whole has a tendency to show square or irregular outlines, and the cell protoplasm is often irregularly serrated at the periphery, as if it was corroded ("angefressen"). Every one of the features characterizing a plasma cell must generally, as we should expect, be lost in karyokinesis. We know that during the process of indirect nuclear division of human cells, the latter, no matter to what specialized type they belong, assume quite a uniform appearance. In a plasma cell undergoing karyokinesis we would likewise expect to see a round cell with a central nucleus rich in chromatin, etc. In sections of the specimen under discussion there are found right in the midst of plasma cells, cells undergoing mitosis. The characteristic and typical figures seen are mostly monospirems and monasters. In one section there is found among plasma cells a large cell with small, scanty basophilic granules and a perfectly regular typical monaster, which, however, does not oc-

2 Ziegler's Beiträge, 1898, xxiv, 163.

cupy the center of the cell, but is found at the periphery at one pole of the cell. At another place there is found a plasma-mast-cell with numerous coarse granules and a karyokinetic figure.

It would certainly be a matter of great interest to be able to demonstrate beyond a doubt that plasma cells which occupy such a prominent place in inflammatory changes were able to mutiply in the tissues in which they are found. It appears now that the plasma cells are derivatives of lymphoid cells, circulating in the blood. Since it is also claimed, and it seems with some good reason, that plasma cells change into fusiform connective tissue cells and finally into connective tissue fibers we would then have a completed circle, starting with the lymphocyte, or plasma cell, migrating out of the vessel into the tissue, being able to here proliferate by karyokinesis, and becoming finally a connective tissue fiber.

Malignant papillary dermatitis or Paget's disease certainly forms an excellent object for the study of the histopathology of inflammation and of the now much spoken of plasma cells, since they do occur in this affection in large numbers. So numerous are they that Unna in describing the case he observed spoke of the "Plasmoma" formed in the derma. It is, however, quite questionable whether the name malignant papillary dermatitis for this disease is a happy one. It appears to us that the division is a true type of carcinoma from the start, one however of a mild degree of malignancy, the extensive spreading of which is for a long time prevented by the protecting wall of cellular infiltration which is formed in the derma. The histologic changes in the latter we think are not to be looked upon as the primary pathologic factor, but as a beneficial protecting reaction. Hence it is hardly proper to derive from the condition in the derma the name for a disease the true etiological factor of which musts be looked for in the epidermis.

April 10, 1899.

A CASE OF OSTEITIS DEFORMANS IN A CHICKEN.

N. W. JONES.

These specimens of chicken bones comprise the long bones of both legs, namely, the femora, the tibiæ with their attached rudimentary fibulæ and the two tarsometatarsals. The remainder of the skeleton was destroyed. In places it is seen that only one side, in others all sides of the shaft of these bones possess large, irregular, rough, nodular growths, which on section prove to be true bony tissue, differing only in that it is somewhat more porous and slightly lighter in color.

The shafts alone are involved. They have lost all resemblance to their original shape on account of this growth, and not because of any particular bending. The extremities are quite normal. Sections show that the medullary canals, excepting in the heads, are much incroached upon, and in places are quite obliterated. The development has not taken place symmetrically, as can be readily seen. The bones of the right leg are uniformly larger than those of the left. The right femur has the greatest circumference in any one place, and the tarsometatarsal of the same side is by far the most deformed. Microscopical sections of decalcified bone show that these new growths possess much the characteristic structure of normal bone. Unfortunately nothing is known of the condition of the skull, nor the other long bones of the skeleton, nor the presence or absence of malignant growths in any part of the body, but the condition of these bones themselves leads one to believe this to be a case of Osteitis Deformans.

April 16, 1899

MISCELLANY.

STATISTICAL REPORT OF DIPHTHERIA CASES TREATED WITH ANTITOXIN IN THE COOK COUNTY HOSPITAL, CHICAGO, FROM JULY, 1895, TO FEBRUARY, 1897.

H. A. BRENNECKE.

The statistics of the cases of diphtheria treated in the Cook County Hospital have never been reported, and they are thought to be of sufficient interest to merit publication. The use of diphtheria serum was begun in July, 1895, and has been continued in conjunction with local treatment since then. The various methods of local treatment recommended have been used with apparently the same result. The medicaments most used were the tincture chloride iron, hydrogen peroxide alone and mixed with an equal quantity of boric acid solution, and a 1-per-cent. solution of bichloride of mercury. During this time the diphtheria service had been under the charge of the late Dr. D. D. Bishop, Dr. A. C. Cotton, and more recently Dr. W. L. Baum.

Laryngeal Cases Treated.—Intubated, 6; died, 1; moribund, 1; mortality, 0. Tracheotomized, 10; died, 9; moribund, 4; mortality, 83.3 per cent. Antitoxin only, 6; died, 1; moribund, 0; mortality, 16.6 per cent. Total cases, 22; total died, 11; total moribund, 5; total mortality, 35.2 per cent.

Most of the cases which were tracheotomized had been previously intubated. Some had been intubated outside of the hospital and entered with a bronchopneumonia,

which accounts for the high mortality. Those cases treated with antitoxin only responded very rapidly and were probably less severe.

The injections have usually been made in the gluteal or lumbar region, and have never resulted in abscess formation. A rise of temperature following the injections was never noted. In thirteen of the 146 cases treated with antitoxin a rash appeared, usually seven to fourteen days after the last injection. Twelve of these were urticarial and persisted three to five days. The thirteenth case was scarlatinal in appearance and persisted two days. The membrane usually disappeared in four and five days, and seldom persisted longer than one week.

According to the various statistics the mortality of diphtheria before the use of the serum is placed at about 40 per cent. Since the serum has been used in the Cook County Hospital the mortality as is shown by the tables has been reduced to 12.4 per cent.

TABLE 2.—July 1, 1895, to February 1, 1897: Treatment with antitoxin according to age.

	0-1 yr.	1-2 yrs.	2-3 yrs.	3-4 yrs.	4-5 yrs.	5-6 yrs.	10-15 yrs.	15-20 yrs.	Over 20 yrs.	Total	Moribund.
Cases	3	18	6	12	10	26	22	12	37	146	
Died	2	8	2	3	3	4	4	1	0	26	8
Mortality, per cent.	66	38.8	33.3	25	30	15.3	18.1	8.3	0	17.8	13

TABLE 3.—Day of disease when antitoxin was injected.

	1st day.	2d day.	3d day.	4th day.	5th day.	Later and not known.	Total.
Cases	15	32	23	17	10	51	146
Died	0	3	5	4	2	12	26
Mortality, per cent	0	9.3	21	23.5	20	23.5	17.8
Moribund, or dying in 24 hrs.	0	1	1	2	1	3	8
Remain	13	31	22	15	9	48	138
Mortality, per cent.	0	64	18.1	13.3	11.1	18.7	13

TABLE 1.—Cases of diphtheria treated with antitoxin from July, 1895, to March, 1897.

	Cases.	Died.	Per cent. of mortality.	Moribund and dying in twenty-four hours.	Leaves.	Per cent. of mortality.	Extent of membrane.				Complications.					No. of Injections given.				Total Injections.	Number of units.
							Tonsils.	Pharynx.	Nose.	Larynx.	Bronchopneumonia.	Nephritis.	Sepsis.	Paralysis	Rashes.	1	2	3	4		
July to Oct., 1895	3	1	33.3	1	2	0	1	0	0	2	0	0	1	0	0	3	0	0	0	3	1000
Oct., '95 to Jan., '96	31	6	19.3	1	30	16.6	16	11	0	4	2	1	3	0	3†	19	7	4	1	49	1000 to 3500
Jan. to April, 1896	23	4	17.3	1	22	13.6	9	5	1	8*	2	1	0	0	4	18	3	1	1	31	500 to 3000
April to July, 1896	25	2	8.	0	25	8.	8	13	0	4	1	1	3	1	1	21	4	. .	. .	29	500 to 2000
July to Oct., 1896	18	7	38.8	4	14	21.4	7	7	1	3	0	1	4	0	1	10	5	1	. .	23	500 to 2500
Oct. to Jan., 1896	36	5	. . .	1	35	13.8	19	9	4	4	2	2	4	2	4	25	7	3	. .	42	1000 to 3500
Jan., 1897	10	1	10.	1	9	0	6	2	1	1	2	. .	1	. .	. .	9	1	. .	. .	11	1000 to 3000
Totals	146	26	17.7	9	137	12.4	66	47	7	26	9	6	16	3	13	105	27	9	2	188	

* One larynx and one nose. † Urticaria.

NOTE.—Since the use of the serum 146 cases have been injected, of which twenty-six died, a mortality of 17.7 per cent. Of these nine were moribund or died within twenty-four hours after admission, which if deducted leave a mortality of 12.4 per cent. The cases of nasal diphtheria had membranes extending to the tonsils and pharynx. In one case the larynx was also involved.

TABLE 4.—Mortality according to age with antitoxin.

	Cases.	Died.	Mortality, per cent.
Up to two years	28	8	42.8
Five to ten years	26	4	15.3
Ten to twenty years	34	5	14.7
Over twenty years	37	....	

TABLE 5.—Mortality according to the day of the disease when injected.

	Cases.	Died.	Mortality, per cent.
First and second days	45	3	6.6
Third and fourth days	40	9	22.5
After fourth day	61	14	22.9

As all cases showing a membrane formation are placed in the diphtheria ward on account of the limited accommodation for further isolation, one injection of 1000 units is given when the patient enters. A culture is made at the same time.

In many of these cases no diphtheria bacilli are found; the patients do not contract diphtheria and do not show any ill effects of the antitoxin.

June 14, 1897.

ANATOMIC RESEARCHES ON YELLOW FEVER.

EDWIN KLEBS.

Yellow fever, a true American disease, originating in the West Indies, is a permanent menace to the United States. So long as unhygienic conditions persist in Cuba, supported by a state of, it seems, permanent revolution and destruction, the southern parts of this land will never enjoy the security so necessary for the development of a general happy state of the population. But it may be asked: Is the terror excited by such invasions and the rigorous quarantine executed in consequence of this feeling of the population really necessary? We have learned in the last years

by a more intimate knowledge of the causes and the manner of infection, that the severest diseases lose most of their danger and cease to excite the population. Relying on the possibility of securing himself against the infection, man will no more relinquish his home in blind terror. I might refer to the "Go-not-away-Club" of Mobile and possibly other localities in the infected parts of the South as a commencement of a deeper and more sure insight into the nature of this disease and infectious diseases in general.

Indeed, modern bacteriologic science has shown us that very few infectious diseases are disseminated through the air. The big fires burning in the streets for the purpose of cleaning the air in times of bubonic pest, are seen no more. Only the quarantines remember this old idea that the person of man is the conveyor of the disease and must, as such, be retained under observation as long as the disease is not broken out.

The more cruel house quarantine, surrounding an infected inhabitant, which prohibits every movement of the persons included, together with the general quarantine, the so-called shot-gun quarantine, has been in general use, in the broadest way, in the last epidemic of yellow fever in the Southern States of the Union; the first exposing the sound members of a household to the infection; the second compelling the well-to-do people to leave the country before they should become prisoners in their own homes.

Science has corroborated the old, popular conviction that the body of the sick contains the germs of the disease and can spread them in different manners, depending upon the parts in which the germs are developing and from the biologic conditions of these germs. No better opportunity for dispersion of germs can be found than in diphtheria, where the bacilli are developing on the surface of the mucous membranes

of the mouth, the pharynx or the nose and throat. Doubtless these germs will be spread around the diseased person by cough and expectoration, but we do not on this account confine the whole family. We have done enough if we seclude the patient in a well aired room and with disinfectants destroy the germs in the immediate surroundings, and prohibit contact with him by other persons except well trained nurses. No other means are needed in typhoid fever and Asiatic cholera.

As to the general quarantine, used for the seclusion of towns and lands, its insufficient character is shown by so many experiences, that no modern hygienist will now advise it. That this measure is only efficient in a few instances in which a despotic ruler secludes himself and his court by closely posted soldiers is shown by the experience of Zarskoje-Selo at the time cholera spread over the world in spite of all quarantines on the frontiers of the different states. Instead of this insufficient quarantine, in the last epidemic of cholera in this decade, the European governments, Germany first, organized a system of medical observation in all directions in which the floating population moved, in the streets, the railroads and the rivers, one observation line following the other at due distance. The infected persons could be detected and retained in a much surer way than by the old fixed quarantine. The same system was executed with full effect in our land when smallpox invaded the South. Why should it not be in a yellow fever epidemic? The answer lies in the blind terror, provoked by this disease, only sustained by our ignorance of the natural manner of the dissemination of this disease. So every addition to our knowledge on the nature of the disease must help to abolish a very natural, but also very dangerous feeling.

To understand the manner of dissemination of yellow fever we must bear in mind the following facts:

1. The disease is transported by sick people, not by goods and not by water. The two latter are absolutely excluded, as no case is known in which it was imported by the products of West India, Central or South America. It is introduced largely in the warmer regions of North America, Africa and Europe. The epidemics in 1817 (Spain Livourne), must have originated by lingering diseases on board the ships. Without this suggestion it can not be understood why the same accident did not occur in our times with a much greater commerce. The few cases that arrive in Europe are promptly caught in the landing harbor; the goods are not infectious.

That water does not act as a propagator of the disease is shown by the fact that an epidemic never follows a river downward, but spreads upward, as in the Mississippi Valley. In smaller towns, as in Mobile, Ala., different centers of infection are formed, in which are found the first cases imported. That was demonstrated to me by Dr. Hermann Mohr, who visited with me all parts of Mobile in which cases of yellow fever had occurred.

2. The personal contagion is not direct or confined only to a very near contact. In many cases of supposed direct contagion the infection was taken up before and in another manner. The best proof for this opinion is given in the recent publication of Dr. Hamilton R. Jones of the Isolation Hospital in New Orleans (JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 1898, No. 9). He writes: "No case of yellow fever was traced to the Hospital in spite of the fact that three of the Sisters had not had it. The ambulance superintendent had never had it, and was frequently covered with black vomit. Fourteen cases passed through the wards, who did not have the disease, none of whom contracted it, and of the army of pioneers engaged in destroying the infected buildings and in

general cleaning up, numbering in all considerably over a hundred persons, not one contracted the disease."

Certainly the greatest antiseptic precautions were taken in the Hospital, but the contagion by the air, this bugbear of yellow fever, favored also by physicians, would not have been excluded by such means.

3. The contagion, emanating from an individual, must be deposited in his surroundings before it can infect other individuals. That this is so is shown by a yellow fever case originating in Whistler (near Mobile), in December, 1897, long after the epidemic in Mobile was extinguished. A workman of the railroad moved to a house in which there had been cases months before, and which had been cleaned and disinfected; there he was infected and died suddenly.

4. The yellow fever often develops very slowly in certain places; the nature of the disease is only detected later, when graver cases follow the lighter ones. So in Ocean Springs, where the first cases were considered as dengue.

The State Board of Health of Mississippi declared that the first case was yellow fever imported from Gautemala in March. The same statement was made in Mobile.

The older observers, as Gérardin of New Orleans (1817), speak of endemic and epidemic forms of yellow fever. The first form was at this time present in New Orleans, as it is now present in Havana, and many places in Central America and Brazil. Near Bahia, therefore, the German-Lloyd steamship line has a station for its sailors, to which they are removed immediately after arrival.

We must conclude from all this, that the disinfection of the sick and their surroundings is fully sufficient to destroy the germs and check the disease.

We now come to the second part of our subject: the germs of yellow fever.

G. M. Sternberg has made a very careful examination of the question and has shown that all the bacteria which he and others before him had found seemed not to be the true causes of the disease. Only when Sanarelli published his researches did he doubt, and think that his X-bacillus was probably identical with the bacterium discovered by Saranelli, inclined to this opinion, it seems, by the apparent results of inoculations made by the Italian author. But in carefully studying the various publications of Sanarelli, I could not suppress some doubts. If the relatively large and slightly stainable bacillus, known as Sanarelli's bacillus icteroides, was the true cause of yellow fever it would be curious if if it had not been detected before. Years ago I had examined preparations received from Rio de Janeiro and could not detect any bacillus in the fatty degenerated liver. Sanarelli could not find his bacillus in every case, which seems strange, if the bacillus is so easily stained and cultivated. Further Sanarelli's is a pronounced water bacillus, and I must accentuate that yellow fever is not conveyed by drinking water. If I had not in younger years fallen into possibly the same error, I would not venture an opposition, the more as I am not quite sure whether Sanarelli has infected men with his bacillus, or only with the toxins prepared from his cultures. I hope the last, for the first experiment would seem to be unjustifiable, the more as it would be futile, if executed in a place in which yellow fever was present. As this may be, I will tell my own error. As I worked, more than twenty years ago in Italy, with Tommasi-Crudeli on the causes of malaria, we found a bacillus in the malarial earth which, cultivated and injected into rabbits, gave intermittent fever with enormous swelling of the spleen. We were very sure that we had found the true cause of this disease, for, what better proof could be thought of than the reproduction or synthesis of such

a characteristic disease as malaria? But we were very soon undeceived by Marchiafava, who as assistant of my friend, had followed our researches. He found the plasmodium in the blood, and it was sustained by that glorious anatomic discovery, the older, but at this time slighted observation of Laveran.

Naturally, in our cultures we had, besides our bacillus, the malaria protozoa, that is as yet not known or even detected outside of the body. Could not the same error occur in the experiments of Sanarelli, as yellow fever is by no means as typic an affection as malaria?

How can we get out of this trap that nature has placed in the way of truth-searching pathologists? Only by anatomic research, which has built up our science, and will accomplish it if perfection is at all attainable; what we can observe with our eyes can not be delusion.

Among the organisms vegetating in higher animals the protozoa or protists seem to play a foremost rôle. They have the property to act as cell parasites. I have shown, as the young assistant of Virchow, that the psorospermia, developing in the epithelial cells of the intestines and the gall ducts of rabbits (seen first by Remak), were living bodies, not eggs of worms, and that they promote, after having penetrated into the epithelial cell, a progressive hypertrophy of these elements. The two constitute a sort of partnership. Much later the plasmodium malariæ, living in the interior of red blood corpuscles, was detected. A third form are the amebæ in dysentery and tropic liver-abscess, on which Kartulis in Cairo (Egypt), and Councilman in Boston, Mass., have done excellent work. These are not intracellular, but appear as the psorospermia (or coccidia) in the passage from the intestine to the liver, a fact that will also be of high value in the study of yellow fever.

As I commenced to study yellow fever preparations, received from Dr. Hermann Mohr in Mobile, Ala.

(from two cases preserved in alcohol; stomach, duodenum, pancreas, spleen, liver, kidney and heart), I thought to try the different anilin dyes in combinations, hoping that if the organs contained foreign organisms these, like the body cells, would have a different power of election for one of these stains.

I was not deceived. First, using mixtures of methylen blue and saffranin, I found a very surprising picture in the liver of yellow fever. But the best results were given by a mixture of seven parts of my parafuchsin kresol solution for tubercle bacilli, mixed with three parts of methylen blue (concentrated solution in borax 5 per cent.), and three parts methylen greeen, 1 per cent. This mixture, which is somewhat thick, can be used full strength or diluted with equal parts of distilled water. If diluted, the staining must be prolonged. The decoloration and differentiation must be made very carefully, if alcohol is used; the blue color of the slice, which should not be thicker than 1/100 millimeter, must never be eliminated. The use of anilin oil and xylol (Weigert) is far better for the decoloration.

If this method is applied correctly, the preparations of the liver give a very surprising picture. Between the lines of the bluish tinged liver cells one remarks intensely stained red masses, oftentimes forming stripes and masses larger than the liver cells. The last are transformed and nearly destroyed by fatty degeneration in the median parts of the acini, and compressed by the red masses, whereas in the center and peripheral parts only isolated red spots are disposed between the liver cells. The red masses consist of round or oval-shaped, or irregular balls which will not conglutinate.

With higher powers, one remarks two constituents of these red masses, very deep stained round, oval or egg-shaped bodies, and slightly stained masses, surrounding the first. Oftentimes in one red mass are

included two or more of these bodies, somewhat larger than a human red blood corpuscle, but oval-shaped and of quite homogeneous structure. It is not difficult to demonstrate that the greater, slightly reddened masses are no other than very enlarged and, in their coloring qualities, deeply changed leucocytes. Oftentimes they contain the blue stained nucleus, somewhat altered, elongated or otherwise deformed. We can seldom detect well conserved leucocytes, which contain the red body included in the blue stained protoplasm. But not all of these red bodies are included in cells. We also find them free between the liver cells, and observe here the largest forms, which measure more than thirteen mikres in length and twelve in breadth, mostly egg-shaped, with one broader and one smaller pole. These contain, mostly, a greater or smaller number of vacuoles and brownish pigment. These larger bodies are not alone situated between, but also in the interior of the liver cells.

When this dislocation takes place, the liver cells show degeneration in the form of clear round spaces, often melting together. If these spaces are filled with fat the left side. If these spaces are all filled up with fat drops it can not be decided, the preparation having been treated with alcohol, but it is not very probable, as the edges of these spaces are not infrequently ragged and irregular. Later only it seems to follow the deposit of fat, converting the whole protoplasm to a network with round meshes.

The question now arises, in what manner do the red bodies penetrate into the interior of the liver cells? If these foreign bodies, as may be suggested, are living organisms, one must suppose that the oval-shaped bodies, first developed in the leucocytes, lying in the interstitial tissue, may divide and penetrate, in their earliest forms, into the interior of the liver cells, there growing more and more; they eat up and destroy the

protoplasm of the liver cell. This destructive process results only in the demolition of the cell substance, which seems, in the commencement of the process, to be somewhat swollen, so that the lines of demarcation, principally in the radial direction, are effaced. The nuclei only show a slight proliferation and usually contain two or more nucleoli, often of excessive dimension.

It is very difficult to decide in which part of the interstitial tissue the oval bodies are primarily deposited. As the gall ducts and vessels seem to be free from them (I found such a body in a thrombosed central vein only once), it must be supposed that they are lying in the lymphatic spaces, which suggestion is supported by the fact that usually where the oval bodies are lying thronged in rows, leucocytes are present in the same spaces, which show the usual form of lymphocytes, with great round, dark stained nucleus and small protoplasm.

Inflammatory processes are observed only in a small extension around the portal veins.

I am not informed as to the general conformation and aspect of the two livers examined, which gave me identical results, but I think that they were of the same aspect as described by Hamilton P. Jones as yellow, dead-leaf or boxwood in color, and bloodless (l. c., p. 460). Possibly they may have been flabby in this stage, with somewhat wrinkled surface; should this be so, the resemblance to some forms of acute yellow atrophy of the liver would be complete. But I will refer the question to the pathologic anatomists who have made postmortems in yellow fever cases. Possibly this affection will show the way to the detection of the true cause of these obscure diseases, so often originating from a seemingly simple catarrhal icterus.

The sharply defined form of these bodies, their dif-

ferent staining, their disposition in the interstitial tissue and in the liver cells, their forming of vacuoles and pigment in the more advanced stages, certainly indicate them to be parasites of the class of protozoa; but, having only dead material before me, I will not decide the question, unless they could be found in other organs in physiologic connection with the liver.

The spleen, pancreas and heart and the blood contained in these organs gave negative results. The stomach and duodenum always show deep alterations in yellow fever. "The mucous membrane of the stomach," says Jones, "was intensely congested, softened and eroded—the duodenum, as a general rule, presented the above conditions, intensified. This condition, however, in the majority of cases extended only down to the opening of the common bile duct" (l. c., pp. 459 and 460). What do our preparations show? We can only say, an intense gastritis and duodenitis, the latter more developed than the former, but the distribution of the emigration foci is of the same character in each. The infiltration of leucocytes always commences around the vessels, penetrating the superficial layer of muscle fibers. In the duodenum these infiltrations are larger and extend oftentimes to the surface of the mucous membrane. But in the two organs the higher parts of the interglandular tissue are filled up with small-edged cells, the nucleus not so deep stained as in the emigrated cells, fibroblasts (Ziegler) or hyperplastic connective tissue cells. The same oval-shaped and red staining bodies were always present in the emigration centers of these organs, not in very great numbers, but never absent. The same were also found nearer the surface, in the hyperplastic part of the interstitial tissue, but seldom in a gland, and if present, were external to the epithelial cells But here another highly interesting form not present in the liver was also found, namely, nearly circular groups

of small round bodies, stained in the same manner as the oval bodies. It may be remarked here, that all these bodies in the duodenum and stomach stain a deeper blue than in the liver. The red color is perceptible only after protracted decoloration.

I might suggest that these blackberry forms represent sporulation. If these spores, developed in the higher layers of the mucous membrane, are set free, they may penetrate into the mucous glands or lymphatic vessels and be transported by the way of the bile ducts or lymphatics to the liver, but this can only be ascertained in a postmortem examination. It seems very probable that the infection is transferred to the liver in one of these ways.

By these observations, to be completed by observation on the living and dead, we can very well understand the source of the disease, which is first a true gastro-duodenitis, remaining such in the milder, lingering or endemic cases of some countries, but the danger of the epidemic form commences with the immigration of the protozoa into the liver.

That the infection with these organisms, showing the nearest relation to coccidia and amebæ, which immigrate into the liver from the duodenum, deprives yellow fever of its terror, is natural, as watery fluids, fruits, vegetables and greens only can be considered as carriers of the infection.

The kidneys are always altered in the graver cases of yellow fever. In 202 cases of yellow fever observed by Jones, albuminuria was found in 125 of the non-fatal, and in all the fatal cases (45), in all 170, or 84 per cent. The amount of albumin varied from a trace to 80 per cent. Yellow stained casts and scanty urine were considered unfavorable symptoms, according to the same observer. The kidneys were generally a "brownish-yellow, larger and softer than normal, loaded with fat, and were generally intensely

congested" (in the medullary substance probably). This is the general aspect in every septic kidney, very similar to the kidney in acute atrophy of the liver.

The microscopic examination shows no inflammation of the kidneys (it is wrong to speak of parenchymatous nephritis in these cases, as there is no proliferation of epithelial cells, nor any migrative process in the interstitial tissue). The convoluted tubules of the cortex alone show alterations, being filled up and vastly distended by a granular exudation; the epithelial cells here are ragged, and often compressed by the exudation. The glomeruli are free, and are also sometimes compressed by the same exudation. In my cases, casts were not formed in so great a quantity as is found in true nephritis.

This affection could be considered as a toxic one, but the differences in the effects on kidneys by true bacteria toxins is very remarkable, affecting the glomeruli in scarlatina (glomerulo-nephritis), and in Asiatic cholera promoting the destruction of the nuclei of the secreting epithelial cells (karyolysis). With exception of the exudation into the glomeruli and tubules, only the fatty degeneration of the cortex in phosphorus and other intoxications resembles this affection in yellow fever.

This condition indicates a true dissolution and hindered oxygenation of the blood, beginning in life; but we should expect then to detect free hemoglobin in the urine.

I will repeat, that this new theory of yellow fever, announcing the affection as a gastro-duodenitis, with consequent atrophy of the liver, originated by certain protozoa, must be supported by the examination of yellow fever patients. I hope to fulfil this task, but think that we will now be better prepared to meet this work of high pathologic and hygienic importance to the United States. March 14, 1898.

AN EPIDEMIC, SEPTICEMIC DISEASE AMONG FROGS DUE TO THE BACILLUS HYDROPHILUS FUSCUS.

FRANK HORACE RUSSELL.

During the last half century or more science has made an extensive use of frogs in her laboratories. they have been used to demonstrate the laws and facts of biology; to ascertain the presence and effect of a variety of poisons; to show the circulation of the blood and the nature of the process of inflammation; to contrast the action of different currents of electricity upon the muscles; to demonstrate the action of curara in destroying the properties of motor nerves. Notwithstanding the close observation to which this laboratory animal has been subjected during recent years, observers have rarely found in it evidence of disease.

In 1891 Sanarelli described and named the organism under consideration. He discovered it while performing some inoculation experiments upon frogs. They accidentally became infected and death soon resulted and this so seriously interfered with his work that he was led to investigate the cause, isolated the bacillus and described the growth of the cultures on plates, glycerin-agar, agar-agar, gelatin, serum, blood serum, and potato. The cold-blooded animals for which the micro-organism was pathogenic were frogs, toads, salamanders, lizards, sunfish and fresh-water eels. Among the warm-blooded animals which died of the infection were guinea-pigs, rabbits, new-born dogs, new-born cats, mice, field mice, chickens and pigeons. The source of the bacillus Sanarelli claims to be in water. Out of twenty-six water-supplies which he examined he found it present in two.

In 1893 the attention of Trambusti was called to this organism because of an extraordinary mortality

among the frogs in the laboratory in which he was experimenting. He identified it with that described by Sanarelli. His investigations in this direction had mainly to do with the physiologic action of the toxic products of the micro-organism upon frogs. He divided his experiments into three lines: 1. The action of the pure culture. 2. The action of those substances soluble in alcohol. 3. The action of those substances insoluble in alcohol. Besides this he investigated the chemic reaction of the muscles, brain and spinal cord of the frog after the injection of the toxic products of the organism.

During the same year the organism was discovered and identified by Rogers. His attention was directed to it because of the death of frogs in the laboratory after the introduction of a fresh lot.

During October, 1897, an epidemic broke out among the frogs kept for experimental purposes at the laboratory of Rush Medical College, and was so remarkable as to demand special attention. The frog tank is a zinc-lined box through which a continuous stream of hydrant water flows. In the bottom were placed some porous rocks of various sizes upon which the frogs could perch and the outlet of the tank so placed that about three inches of water continually remained in the tank. At the beginning of the school year a new supply of sixty frogs was put into the tank along with eighteen which had been kept over from the preceding year. In a short time they began to die and during six days about seventy perished, while not many days passed before the remaining ones died. The tank was then thoroughly sterilized, the sharp-cornered rocks replaced by boxes of sand, and a new lot of frogs put in. A few of these died, but by removing the affected ones as soon as any symptoms developed the remaining ones have been fairly well protected.

The symptoms following infection commenced with

a disinclination to move. When touched on the end of the nose there was not the customary response. Along with this lassitude there was swelling of the abdomen, which varied somewhat as to degree. There was also more or less change in color. The dark greenish hue faded to a greenish-yellow tinge; especially was this marked around the black spots on the back. The change in posture was noticeable. The animal changed from a semi-erect position to a horizontal. The head was not held up but carried on the same level as the body. Rather late in the infection the legs were thrown out from the body. The fore legs had their palmar surfaces directed outward. The hind legs took a position about at right angles to the body. When urged the frog did not jump but tried to get along by a creeping movement. During this stage swimming was difficult. Shortly before death muscular contractions were observed, during which the hind legs were thrown as far forward as the head. These spasms were of short duration but recurred. Toward the end of the disease there was coma and during this stage all outward signs of life disappeared. The body showed no rigidity and remained in any position in which it was placed. When the thorax was cut open the heart was found still beating.

At least sixty frogs were examined postmortem. All of these presented practically the same lesion whether infected spontaneously or inoculated with cultures.

In making the examination the following precautions were taken: To prevent contamination all instruments were sterilized with heat. As each cavity was opened inoculations were made on various media and at the same time cover-slip preparations were made. Each organ was examined in the same way. Cultures were made upon the different kinds of media but in addition to this, provision was made to grow the organism in the absence of oxygen. The tissues from all the organs and from the muscles were preserved for

sectioning. The hardening fluids used were alcohol, corrosive sublimate, formalin and Mueller's fluid.

The following is a résumé of the most important findings in the examination of the dead bodies: The tongue in most cases had hemorrhagic spots upon its upper surface. The muscles, especially those of the thigh, contained more or less infiltration of blood. The appearances varied considerably; sometimes there were only a few spots which were large in size, one was observed which was nearly the size of a pea, sometimes the points of hemorrhage were very small and thickly set. In this form all the muscles of the legs and abdomen were distended. An incision revealed a serous blood-stained fluid, found subcutaneously and in all the cavities of the body. In quantity this was relatively large, especially in the abdominal cavity. The lungs were sometimes distended with air but more often collapsed. The heart muscle was pale and flabby. The stomach and intestines were markedly distended. The blood vessels on their surface were much congested. Upon opening these viscera a large amount of jelly-like material was seen. The spleen was soft and contained considerable blood, the liver dark brown in color and of a mottled appearance. It was soft in consistence. The gall-bladder contained considerable greenish-yellow fluid. The kidneys were negative. In the bacteriologic examination, cultures were obtained from all the organs and cavities of the body. Cover-class preparations showed a large number of bacteria. The organism was a bacillus (Fig. 3), in shape short and thick with rounded ends. It appeared at times almost egg-shape. Its size in the cultures varied greatly according to age. When examined from the fluids of the body the characteristic appearance was in twos joined together end to end. Occasionally bacilli appeared isolated and at times short chains were seen, and sometimes a number are clumped together.

CULTURES OF DIFFERENT MEDIA.

1. *Agar-agar plates, twenty-four hours old.*—In shape the colonies are round, edges well defined, and regular with a few indentations about the periphery. Usually a dark spot appears in the center. The culture as a whole presents a granular appearance. In color it has a slight bluish tinge when viewed with the unaided eye. Under the low power of the microscope it is yellowish. On the second or third day a ring appears about midway between the central dark spot and the periphery, which encloses a darker colored area.

2. *Plates on gelatin, twenty-four hours old.*—The colonies are yellowish in color and uniformly granular, the edges are well defined but a little ragged. After the second day they can not be studied to any advantage because the gelatin is liquefied.

3. *Cultures on agar-agar slants.*—The organism grows rapidly on this medium appearing first in three or four hours as a whitish gray line along the streak of the needle. The edges often show round colonies which possess a pearl-like glistening. In its growth it becomes raised above the surface of the medium and spreads slowly from side to side. In two or three days it turns to a dirty gray, gradually changing to a dark amber color which becomes more pronounced with age. This amber color is not only present in the cultures but also becomes diffused through the medium. There is a radiating appearance to the culture with a narrow zone about the edge which is light in color.

4. *Blood serum.*—Examined after twenty-four hours it shows an ash gray color. The growth is quite spreading with undulating edges. In the bottom of the tube is a quantity of fluid due to the liquefaction of the media. This is cloudy, resembling the growth in bouillon. The growth looks milky and is partly undermined at the edges.

5. *Glucose agar, stab culture, twenty-four hours old.*—On the top there is a growth about the point of puncture. Along the track of the needle and branching from each side are many gas bubbles.

7. *Bouillon, twenty-four hours old.*—The fluid is diffusely clouded. When shaken slightly it is seen to contain a grayish-white sediment which looks like rolling clouds. In the bottom there is quite a collection of the same material. A characteristic odor is present which is a combination of two odors, a slightly fetid and an aromatic odor.

8. *Glycerin agar, twenty-four hours old.*—Here a white line appears along the track of the needle. The growth does not tend to spread much. There is a slight bluish fluorescent at the edges. The growth is slow and does not turn dark, as is the case on the agar-agar. The color of the media remains unchanged.

9. *Litmus milk, twenty-four hours old.*—Nearly the whole of the contents of the tube is coagulated. The color is light purple. After forty-eight hours the coagulum has become much firmer and reduced in size until fluid and coagulum are about equal in quantity. The color of the fluid now becomes cherry-red.

10. *Gelatin stab, twenty-four hours old.*—A grayish-white growth appears along the whole path of the needle. At the top there is a depression of liquefaction about the size of a pepper seed. Gas bubbles often appear along the needle track. At forty-eight hours there is liquefaction at the top, the size of a pea, with more or less liquefaction along the whole neede track. In about four days liquefaction is complete.

11. *Potato, twenty-four hours old.*—The growth when turned toward the light is glistening. At first it is straw-colored; if any portion of the potato is somewhat dry, the growth here is orange yellow. It does not show much tendency to spread. The outer edge is irregular. Many raised points can be seen resembling blebs. Ex-

amined forty-eight hours after inoculation it has a dirty appearance. The blebs become more prominent. On the fourth day the growth begins to take on a chocolate color which resembles the growth of the bacillus of glanders.[1] The brown color becomes more marked with age.

Cultures do not die readily. They will live at least five months upon media without being transplanted.

LETHAL TEMPERATURE.

The bacteria are killed by a temperature of 50 degrees C. in from five to eight minutes. The method employed to determine the point of thermal death was as follows: A boullion culture was put into small sealed glass tubes. These were put into water maintained at a temperature of 50 degrees C. At different intervals these were removed. broken open and inoculations made into media. Five minutes at this temperature greatly retarded the growth and eight minutes was sufficient to kill them. Cold will not kill them. After being exposed for seventeen hours at a temperature of —20 degrees C. they still grew when put into the incubator, though their growth was greatly impeded.

MOTILITY.

The organism examined by means of the hanging drop exhibits active motility. It has the power of both backward and forward motion. If its movements are watched, frequently it will be observed to start in a certain direction, stop suddenly, and without turning to go in exactly the opposite direction.

REACTION TO STAINS.

It does not stain by Gram's method, but takes the other common stains readily. Methylene blue makes a very distinct and convenient stain. For blood prepara-

[1] This is easily differentiated from glanders by the use of a saturated solution of mercuric chlorid. A few drops added to the culture turns the bacillus of glanders to a bluish-green color which persists several days. A few drops of the solution added to the bacillus hydrophilus fuscus turns it to a milky-white color. In the latter the original color returns after a short time.

tions a simple and easy process of stainng is by the use of eosin and methylene blue. The red blood cell is stained light green, the nuclei of the red and the white blod corpuscles together with the bacteria are stained blue.

Another method used for studying the action of the bacteria in the blood is the following: A staining solution is made by adding methylene blue to a physiologic salt solution to the point of losing its translucency. A wall of vaselin is made on the slide inclosing an area somewhat smaller than the cover-glass and into this a little fresh blood is put with two or three drops of the staining solution. The cover-glass is put on and the preparation examined under the immersion lens. The blue readily stains the bacteria, the leucocytes and the nuclei of the red blood corpuscles. The bacteria can be seen moving in the midst of the corpuscles. Some are isolated and move rapidly; others show chain formation and are sluggish. Occasionally a leucocyte is broken down and is seen to contain bacteria.

FLAGELLA.

Flagella (Fig. 4) were demonstrated by the use of a modification of Loeffler's method of staining. Cultures on agar four or five hours old gave the best results. The older bacilli do not show any flagella. A platinum wire was flattened out for the purpose of touching the culture without geting any of the media. This wire was then introduced into a small quantity of distilled water when a string of bacteria could be observed leaving the needle. A very fine capillary tube was then filled with this water containing bacteria and very fine drops placed on a slide previously cleansed with alcohol and acid and then heated to a redness. When dry the slide was fixed in the flame in the ordinary way. The mordant was applied and the slide held high above the flame (no alkaline or acid solutions were used). After steaming the slide was washed with distilled water and then alcohol. Carbol-fuchsin was then added and heated to the point

of steaming. The slide was then washed, dried and mounted. By this method it was ascertained that the organism has but one flagellum. This is attached to one end. It appears wavy and is from four to six times the length of a bacillus.

INOCULATION EXPERIMENTS.

1. Frogs were inoculated in the thigh, in the peritoneum and in the lymph sac on the back. They gave no symptoms additional to those already given in describing the epidemic disease, except occasionally after inoculation a frog would have a paroxysm of coughing during which a frothy fluid would come from his mouth. After these inoculations with virulent cultures death ensued in from eight to sixteen hours.

2. The rabbit was inoculated into the ear vein; this produced death in a little over two days. The inoculated ear was enormously swollen and drooped to the floor. Upon examination no exudate was found subcutaneously; a slight amount of blood-stained fluid was in the abdominal cavity, also in the pleural cavity. The heart contained much darkly colored blood; the liver, spleen and kidneys were congested; the stomach and intestines were distended with gas; the bladder was full of urine; the lungs were normal. Muscular hemorrhages were not noticeable. One of the rabbits that was used had been made immune to pus microbes. It was inoculated in the abdominal cavity, also in the vein of the ear. Each time it became sick but resisted the infection.

3. The guinea pig was inoculated in the abdominal cavity. In about an hour it had a severe chill; in another hour it became restless, breathed rapidly and showed evidences of fever; in three or four hours after inoculation it became very weak and continued in a state of prostration until death, which occurred eight hours after inoculation. The internal lesions were practically the same as in the rabbit.

4. The house mouse was inoculated in the abdominal

cavity with a culture from agar-agar shaken up with a little bouillon. Soon after inoculation the mouse became very restless, ran about the cage and scratched itself. Later it shivered and soon went into a prostrate condition and died two hours after inoculation.

5. The white rat died five hours after inoculation. The symptoms were shivering, bristling of the hairs, and later prostration.

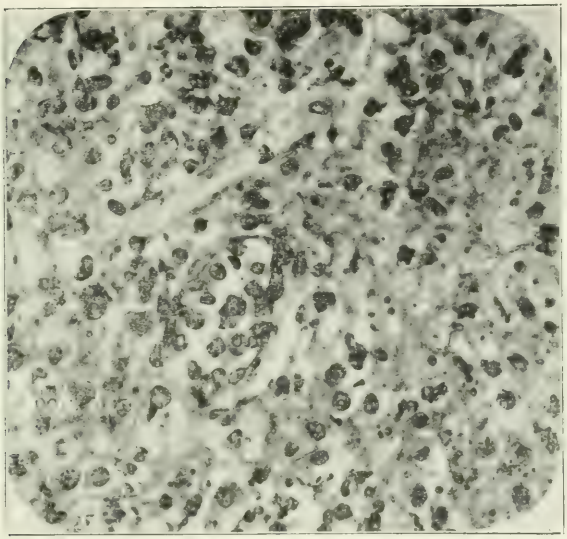


Fig. 1.—Necrosis in spleen of a frog. Stained with hematoxylin and eosin (x200).

6. Two different pigeons were tried. They were inoculated in the breast and the axillary veins. They became sick after each inoculation but resisted death.

EXAMINATION OF THE TISSUES MICROSCOPICALLY.

1. Frog.—The tissues were stained with hematoxylin and eosin and with methylene blue. The spleen shows evidences of marked congestion. Through the organs there are areas of retrograde changes and areas of congestion: *a*. The areas of retrograde changes differ much

in size and shape and are always irregular. The groundwork consists of a granular eosin-staining material not uniform in thickness. Around the heavier staining material are spaces of less density. This groundwork is thickly studded with hematoxylin staining material, especially where the groundwork is less dense. This hematoxylin staining material, incuding nuclei and their fragments, exhibits a great variety of forms and staining properties. There are lightly staining nuclei more or less enlarged. The outline stains dark and the center light. Within the nucleus the chromatin is collected in granules which have a tendency to collect in bunches around the periphery. Although these nuclei in places are regular and round in outline, they are mostly irregular and abnormally shaped. They assume a large variety of shapes, pear shape, dumb-bell shape, crescent shape, K shape, spiral shape. Some are ragged in appearance where one side of the nucleus has disappeared. Another variety of nuclear substance is bodies which stain very deeply with hematoxylin, homogeneous in character, resembling a fused mass. In size they vary from those just visible to the size of a red blood corpuscle. They are globular in shape. Resembling these globular bodies are oblong bodies, but which do not show the difference in size. They have a tendency to mass and sometimes are arranged slightly star shape. Another variety is irregularly shaped dark granules. These do not stain evenly, are accumulations of granules of chromatin, very ragged in outline and joined together in many ways, not infrequently cauliflower in shape. In these areas of nuclear fragmentation a few isolated red corpuscles appear. Some fields contain more than others, but they are comparatively few. Many of the corpuscles are distorted in shape (Fig. 1). Sections stained with methylene blue show that these fields contain many bacilli, frequently distributed in clumps. Stained with Weigert's fibrin stain, minute bands of

fibrin run in all directions inclosing the nuclear granules in a delicate network. In the necrotic areas there are many hematoidin crystals, appearing as isolated single crystals and also collected in masses. *b*. The congested areas.—The congestion in these areas is intense. So compact are the blood corpuscles that no spleen structure can be seen except at the edges of the areas. Here the blood fills the lymph spaces and infiltrates the tissues.

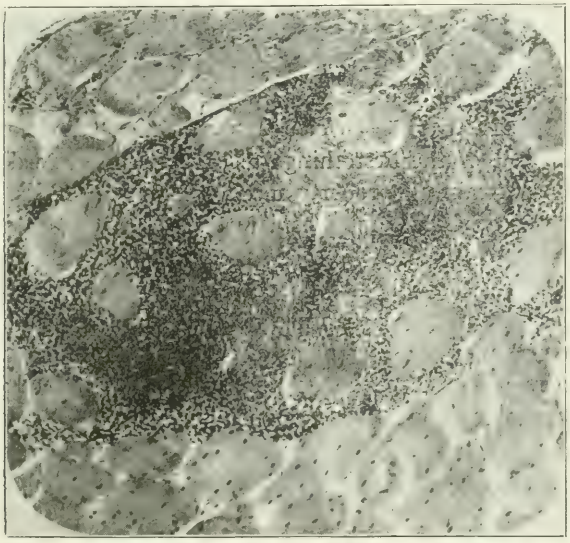


Fig. 2.—Intermuscular hemorrhage in the thigh of a frog (x 200).

The muscles present changes of interest. Those of the thigh were examined. In looking at a cross section a number of areas are observed showing retrograde changes in the muscular fibers. These are always accompanied with hemorrhage. The changes in the fibers are of two varieties: *a*. Through compression.—In the densely congested areas the muscular fibers undergo pressure atrophy. Some have become so small that only a delicate band is left. These may show further retro-

grade changes or may not. *b*. Degeneration.—The changes seen are separation of the fasciculi from one another, accompanied by a wavy appearance. The crossed striæ disappear. The fibers refuse the eosin stain and are dark yellow in color. Subsequently the nucleus disappears and there remains only a mass of granular débris. Fibers are then seen in all stages of degeneration. An individual fiber may be observed in which a part may be undergoing a retrograde change and the remainder be little affected (Fig. 2).

The lungs and kidneys show little or no change.

In the liver marked changes occur. The retrograde process is of a diffuse character in which the whole liver participates. In comparing this with the normal liver one of the first things to be noticed is the difference in staining property manifested by the cells. In the place of the protoplasm taking the eosin stain exclusively, as in the normal liver, it takes the mixed stain. The cell bodies do not stain evenly. The protoplasm has the appearance of a bunching of granular material so that some parts of the cells are denser than others. This often affects the contour of the cell; the edges are often irregular and ragged; sometimes no distinct cell outline can be seen at all; sometimes the outline of the cell stains rather deeply while the center shows little remaining cell matter and the nucleus, if it has one, appears free. In the protoplasm of the cell are many darkly stained granules. In a single cell there are from one to eight or ten. These differ in size from those barely visible to those one-tenth the size of a normal nucleus. They do not occupy any special place in the cell. The nuclei of the cells show all stages of degeneration. They have suffered far less, however, than the cell bodies. Some of the nuclei appear bladder-like and contain little chromatin, others show a mass-like accumulation of chromate granules about the edges, often located almost exclusively on one side. The nu-

cleus frequently loses its round contour and becomes elongated, assuming many shapes. In some of the cells the nuclear membrane has disappeared leaving an irregular mass of chromatin granules. The capillaries are dilated and contain considerable blood, together with cell detritus and fragmented nuclei. The walls of the capillaries are broken in many places and the blood corpuscles have escaped among the cells. Bacteria are found in abundance in the capillaries, appearing usually in bunches and often occupying many of the broken down cells.

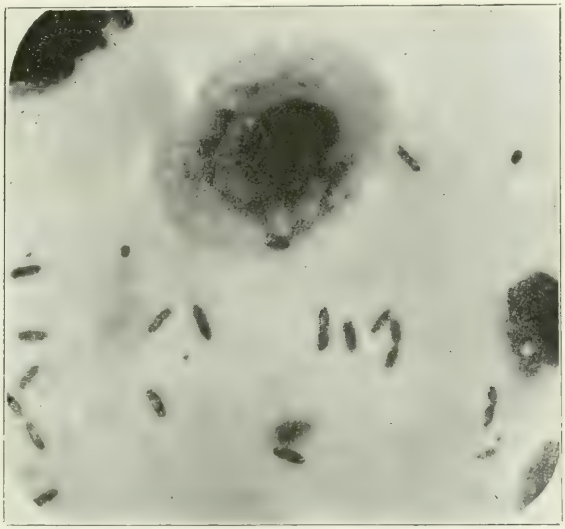


Fig. 3.—Bacilli in blood of frog. Stained with methylene blue (x 200).

Cross sections of the spinal cord and brain show that these organs do not escape the destructive action of these agents. Quite extensive necroses occur in both places. When sections are stained with methylene blue bacteria appear in abundance in these tissues. The minute study of the lesions and effects of the toxins on the nervous system will be deferred to a subsequent time.

In frogs, where infection has lasted several days the lymph sac on the back shows great changes (it is here that inoculations were made). In the recent state the sac is quite well filled with jelly-like material. In character it is a rather soft, semi-transparent mass which can easily be squeezed between the thumb and finger.

Microscopic sections show that these growths are attached to the inner surface of the skin. They appear pedunculated. A cross section of one of these masses shows a dark center and a light periphery. Blood vessels are present. The vessel walls are thin and lined with flat endothelial cells. With high power the dark center is seen to be made up of a large aggregation of nuclei and nuclear fragments, mostly the latter. There are dark granules which are round, oblong and irregular, together with a great number of very fine granules. Mixed up in this mass of broken down nuclei are a few red blood corpuscles, many leucocytes and a few lightly staining nuclei distorted into many shapes.

The periphery shows a somewhat reticulated structure which to some extent enters into the formation of the dark center described. In this eosin staining groundwork are a few blood cells with a few nuclei and granules.

Fibrin is present in these structures, as is shown by Weigert's fibrin stain.

2. Guinea-pig. The tissues of the guinea-pig show evidences of an infection, although the time between the inoculation and death was only eight hours. The spleen and liver contain most of the changes. The muscles, testicles, lungs and heart do not present any marked pathologic conditions. *a.* In the spleen a strong contrast exists between the Malpighian corpuscles and the spleen pulp on account of the large amount of blood in the latter. In looking over the specimen with the low power many dark spots appear scattered

through the pulp. These areas are relatively small, contain a granular center and are full of bacteria. Surrounding this there is quite an extensive zone consisting of leucocytes more or less broken down, and nuclear fragments. The pulp is everywhere greatly congested with blood. The Malpighian corpuscles show no changes. *b*. The liver also shows many focal necroses. These do not choose any special part of the lobule by preference. They are mostly small in size, some so

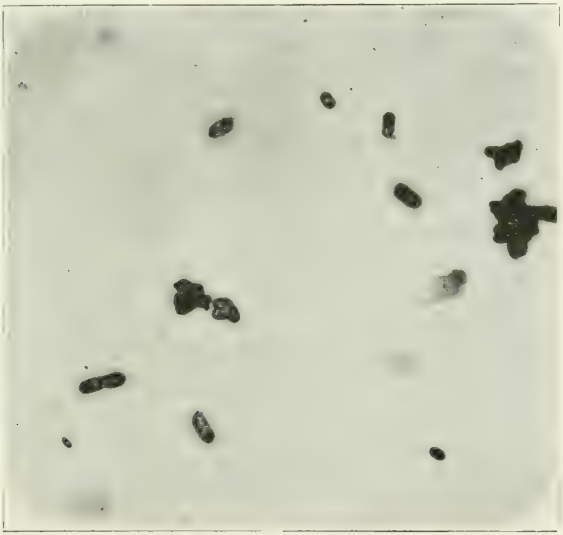


Fig. 4.—Flagella (x 1200).

minute as to occupy only one liver cell. The central part is finely granular and stains darker than the liver cells. In the process of disintegration the cell body comes to show the first change, which is a granular appearance. The outline becomes irregular and ragged. The chromatin of the nucleus, which soon shows changes, collects at the periphery in masses. Frequently it is nearly all on one side. The circle becomes broken and the nucleus as such disappears. The cells through the liver have

a more or less granular appearance. The edges are not easily made out and their nuclei do not stain evenly. The capillaries are dilated and contain many cell fragments and granular material.

3. Rat. *a.* Liver.—In looking over the specimen one of the first things to attract attention is the large number of leucocytes which it contains. These are often gathered in masses. The liver cells contiguous to this round cell infiltration may or may not be affected. In not a few places the liver cells have undergone disintegration. Away from these areas the liver cells do not show any particular change except the granular appearance of its protoplasm. *b.* Spleen.—The most noticeable feature is the congestion. The Malpighian corpuscles appear very prominent. The lymph spaces are greatly crowded with blood. In a few of the Malpighian corpuscles some infiltration has taken place. In a few areas there is cell fragmentation about the edges of the Malpighian corpuscles. In them we see lymph cells which stain lighter than usual. They have lost their normal shape and many appear vacuolated. Nuclear fragments and bacteria are found in large numbers in these areas. *c.* Kidney.—No marked changes are to be seen except in the veins and convoluted tubules. In some of the large veins there can be seen breaks in the walls. Here the blood infiltrates the tissues, accompanied with a dissolution of the contiguous tubules. At the junction of the vein with the tissues there are fragmented nuclei. Some of the nuclei of the vein can be seen free, still retaining their natural shape. The lumina of some of the convoluted tubules are very irregular and ragged. *d.* The muscles, stomach and heart muscles show no change. *e.* The lungs show no changes except a moderate congestion.

4. Rabbit. *a.* The spleen shows much congestion. In the pulp a large amount of hematoidin crystals exist, isolated and in masses. The Malpighian corpuscles show

little change and are not infiltrated to any extent. There are no focal necroses. *b*. Many of the liver cells appear rather narrow, surrounded by distended capillaries filled with blood. They are granular in appearance. In places much of the cell body has left the nucleus, leaving it almost and sometimes quite free. Some of the nuclei have assumed abnormal shapes. The capillaries contain protoplasmic and nuclear ma-

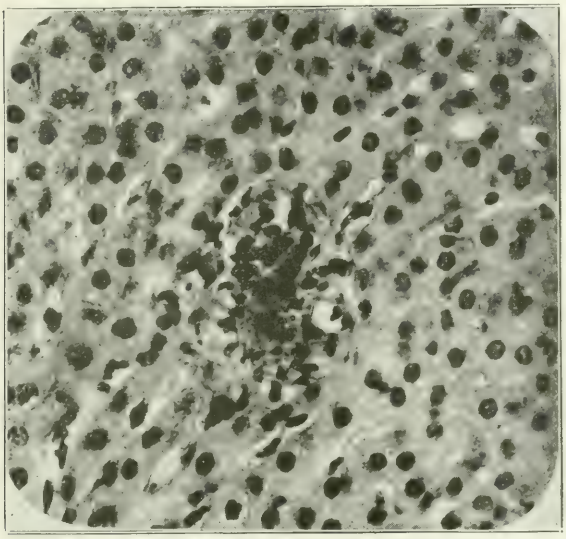


Fig. 5. -Focal necrosis in the liver of a guinea pig (x 200).

terial mixed in with the blood. Liver cell nuclei, having more or less surrounding protoplasm, can be seen distinctly in the lumina of the capillaries. In many of the large veins and in many of the central veins of the lobules can be seen free bodies consisting of eosin staining material in which are mixed darkly staining granules. There are no areas of round cell infiltration. Throughout the specimen are scattered a large number of hematoidin crystals. *c*. In the kidney the convoluted tubules show granular changes and stain irregularly.

The lumen contains granular material, epithelial cells and nuclear fragments. There are no focal necroses and very little congestion. *d.* The muscles and stomach show no changes. *e.* In the brain the most noticeable thing is the congestion of the blood vessels.

5. Mouse. *a.* The liver shows focal necroses which answer in description to those found in the liver of the guinea-pig. The liver cells are granular. Many of the nuclei have lost their shape and show different forms. In the capillaries there are cell fragments consisting of cell protoplasm and nuclear granules. Small masses are present in the large vessel as was described in the liver of the rabbit. When stained with methylene blue bacteria appear in large number in the capillaries. *b.* The testicles, epididymis and heart muscle are negative. *c.* The kidney is very similar to that described in the rabbit.

A fact to be noted in the examination of the tissues is the relation of the virulency of the organism to the focal necroses. As a culture grows old it becomes less virulent. Virulency is best retained in the blood taken from the heart and kept in sealed tubes. When a culture which is two months old or more is injected into the frog, sickness is produced which rarely results in death. Thus different grades of virulency can be observed. If after an inoculation with a culture attenuated by age a frog survives two days or more, no focal necrosis may be expected. The congestion in the organs remains about the same, except less marked. The exudation into the serous cavities is also less noticeable. This same relation between the degree of virulency and the amount of lesion holds true with the warm-blooded animals. The greater the virulency the greater the amount of necroses.

As to the mode of infection nothing definite can be stated. If bacteria are put into water and into this is introduced a frog having a cutaneous lesion, infection

will take place. Several times frogs which supposedly had no cutaneous erosions were put into infected water and only one died. In this case it would be impossible to prove that no lesion of the skin existed. Bouillon cultures of the organism on several different occasions were introduced into the stomach by means of a glass tube, but with no apparent effect. It seems very probable, therefore, that the sharp-cornered rocks in the frog tank had much to do with the original epidemic. The

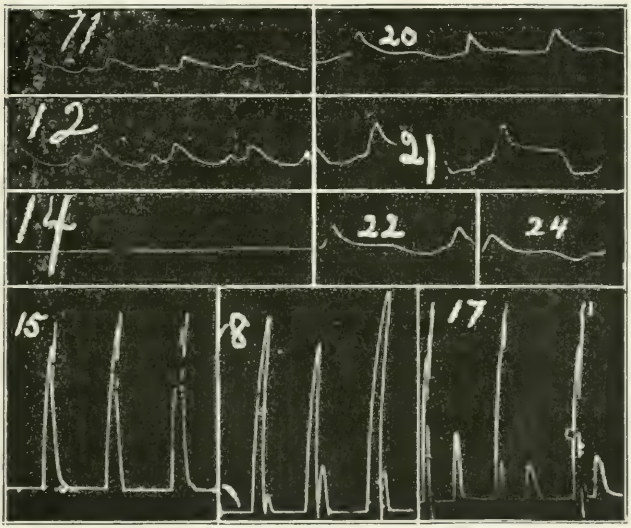


Fig. 6.- 20, tracing with the cardiograph of the frog's normal heart beat. 21, five minutes after injection of toxins insoluble in alcohol. 22, fifteen minutes after injection of toxins insoluble in alcohol. 24, thirty minutes after injection of toxins insoluble in alcohol. 15, contraction of normal gastrocnemius muscles. 18, gastrocnemius muscle one-half hour after injection of toxins insoluble in alcohol. 11, tracing of normal heart. 12, ten minutes after injection of toxins insoluble in alcohol. 14, thirty minutes after injection of toxins soluble in alcohol. 17, gastrocnemius muscle thirty minutes after injection of toxins soluble in alcohol.

frogs gliding over these sharp projections could easily sustain injury of sufficient extent to admit of the entrance of the bacteria.

The source of the bacillus is yet an open question

During the epidemic, bacteria were found in great numbers in the water of the frog tank. It has been ascertained also that a frog inoculated with the bacillus will infect the water. It is evident, therefore, that there might be two ways to explain the source of the organism. The bacteria might be in the Chicago water or they might come with the frogs. The tap water has been examined several times with negative results. A frog, in which was kept an open wound, was put into running water and retained there for two weeks. No infection took place. It is most probable, therefore, that the bacteria came with the frogs.

Widal's test was performed on two different occasions. Frogs were used which were at the point of death. The serum was diluted thirty times and no agglutination took place. With five to ten dilutions there was agglutination, which after a few hours in a warm place disappeared. At another time forty dilutions were made with no clumping of the bacteria.

TOXINS.

In order to test the toxins a culture of bouillon was placed in the incubator at a temperature of 37 degrees C. and left to grow for three weeks. This was then filtered through a Chamberlain's filter. When 2 c.c. of this filtered fluid was injected into the lymph sac of the frog no effect whatever was produced.

Dead bacteria were also injected into a frog. This produced some indisposition which was shortly recovered from.

This filtered bouillon culture (following Trambusti's method) was subjected to farther processes in order to get the toxins in a more concentrated form. To about 115 c.c. of this fluid 290 c.c. of absolute alcohol were added. With occasional shaking the alcohol was left in contact about two days. Then this mixture was filtered through two thicknesses of filter-paper. The filter-paper was then dried and washed with 22

c.c. of distilled water. This constitutes the toxins which are insoluble in alcohol. The fluid which passed through the filter was evaporated in a water bath. Then 30 c.c. of absolute alcohol were added to the residue so as to precipitate all the toxins which were not soluble in absolute alcohol. This was filtered and the filtrate evaporated a second time. This last residue was then dissolved in 15 c.c. of distilled water. Thus two classes of toxins were obtained, those which are insoluble in alcohol and those which are soluble. When these toxins are injected into frogs marked effects are produced.

1. *Toxins which are insoluble in alcohol.*—A frog was prepared in the usual manner and a tracing of its normal heart taken by the cardiograph (Fig. 6). Then 1 c.c. of the solution of the toxin was injected into the lymph sac of the thigh and also into the peritoneal cavity. Five minutes after injection a tracing was taken (Fig. 6). The horizontal distance through which the lever moved was twice that of the normal. Diastole was prolonged. The tracings also show a retarded action. The following table shows the number of beats injection:

Time.	No. beats.
11:17	35
11:25	31
11:46	28
1:01	22
1:07	17
1:12	heart stopped in diastole 4 or 5 minutes.
1:27	5

About two hours after injection the action of the heart became peculiar. It would stop in diastole for four or five minutes. Then it would begin to beat again The rate was slow, being only five to eight times per minute. After six to thirteen beats it would again stop in the same way. Although the rate was very slow, every beat was forceful. The ventricle contracted so firmly as to become white.

Tracings made by means of the myograph on the

gastrocnemius muscle showed changes which can best be seen by comparing Figs. 15 and 18. A short curve appears immediately after the long curve; then a straight line follows until the next long curve.

2. *Toxins soluble in alcohol.*—The frog was prepared and treated in the same way as already described (Fig. 11). Ten minutes after injection there was no variation in the curve except it was stronger (Fig. 12). The rapidity of the heart was the same. Thirty minutes after injection the action of the heart was so feeble that practically a straight line was obtained by the cardiograph (Fig. 14). Thirty minutes after injection the gastrocnemius muscle showed a decided variation from normal (Fig. 17). The down stroke of the major curve is continued below the basement line, then arises a little above it and falls again to the basement line. Half way between the major curves is a short curve. Thus we have two toxins produced by this organism, each having a powerful effect upon both the voluntary and involuntary muscles. (A more extended study of the toxins in connection with the nervous system is reserved for a later date.)

It is quite evident that the cause of our epidemic in the frog pond is identical with that described by Sanarelli, Trambusti and Rogers. Our experiments have very similar conclusions to theirs, but a few things have been added. In looking over the literature there is no record of necroses observed in the organs, the flagella had not been studied, the thermal death-point had not been ascertained, and no observations had been noted in relation to the degrees of virulence. Two differences are to be noted between Saranelli's organism and ours: we fail to get gas bubbles in the substance of the media after inoculating a slant of glycerin-agar, unless the needle penetrated it. Another difference is in the inoculation experiments with the pigeon. Here infection by an intravenous injec-

tion produced sickness from which the pigeon recovered on the second day; in his case it died.

To sum up, we have been studying a water organism, a short thick bacillus with rounded ends, which possesses active motility and has but one flagellum, is chromogenic, gas-producing and aerobic, but grows also to some degree without oxygen. It grows well upon all culture-media. Gelatin is liquefied, bouillon diffusely clouded, upon agar-agar there is produced in a few days an amber color which also colors the media, potato produces a chocolate-colored growth, litmus-milk is made acid, glycerin agar produces an ash-white growth but does not change in color and glucose-agar shows gas formation. It grows best at body temperature and does not stain by Gram's method.. The cold-blooded animals for which it is pathogenic are frogs, toads, salamanders, lizards, sun-fish, and fresh-water eels. The warm-blooded animals which succumb to infection are guinea pigs, rabbits, new-born dogs, new-born cats, common mice, field mice, bats, chickens and pigeons (Sanarelli). The virulence of the organism varies greatly. Cultures gradually lose their virulence with age, but blood taken from the animal and sealed in tubes will retain it for months. Infection produces a septicemia. Warm-blooded animals are seized with shivering and restlessness, followed by prostration and death. Cultures can be obtained from the blood and from all the fluids and organs of the body. Exudations of blood-stained fluid occur in all the serous cavities, especially marked in the peritoneum. Histologic examinations reveal focal necroses in the spleen, liver, brain and spinal cord with congestion in the other organs. In the frog, intermuscular hemorrhages occur with destruction of muscular fibers. The organism produces powerful toxins which were divided into two classes, one resembles in its action digitalis and the other veratrin.

April 11, 1898.

BIBLIOGRAPHY.

Sanarelli: Ueber einen neuen Mikro-organismus des Wassers, welcher für Thiere mit veränderlicher und konstanter Temperatur pathogen ist. Centralblatt für Bakteriologie und Parasitenkunde, B. 14, 1891.

Trambusti: Ueber die physiologische Wirkung der Stoffwechselproducte der Hydrophilus Fuscus. Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie, B. 14, Heft 2, 1893.

Rogers, M.: Une épizootic observée chez dez grenouilles. Comptes rendus de la Soc. de Biologie, 1893.

THE FATE OF THE GIANT CELLS THAT FORM IN THE ABSORPTION OF COAGULATED BLOOD SERUM IN THE ANTERIOR CHAMBER OF THE RABBIT'S EYE.

LUDVIG HEKTOEN.

In this article it is the purpose to describe briefly the results of some experiments which show that the multinucleated giant cells which form during the absorption of foreign bodies in the tissues may divide into viable cells.

Concerning the extensive literature about giant cells—their formation, function and fate—reference is made to an article by the writer entitled "The Fate of Giant Cells in Healing Tuberculous Tissue as Observed in a Case of Healing Tuberculous Meningitis,"[1] in which it is pointed out that giant cells in tuberculous tissue, under certain conditions, undergo progressive changes and separate into small living cells.

THE EXPERIMENTS.

Small pieces of sterile, solidified blood serum, such as is ordinarily used as a culture medium, were inserted under aseptic precautions and cocaine anæsthesia into the anterior chambers of several healthy rabbits' eyes through a small incision in the sclera near the corneal

[1] Journal of Experimental Medicine, 1898, iii. 21.

margin. Once a bit of sterile potato was introduced. These operations were skilfully made for me by Dr. Cassius D. Westcott, Instructor in Ophthalmology in Rush Medical College, and I wish to thank him for his kind aid.

After perfecting the technique the operations were followed by but little reaction; in some instances the vessels in the sclera were congested for three or four days, the cornea rather cloudy, the anterior chamber turbid, and more or less photophobia was apparent. Soon after their implantation a small greyish white rim would become visible around the foreign bodies, which gradually disappeared until, if allowed, only a small, greyish, semi-opaque thickening in the inner surface of the cornea remained. In a few cases the blood serum was gradually dissolved without any accumulation taking place around it, the cornea and anterior chamber remaining perfectly clear. In the case of the bit of potato and when pieces of dry and hard serum were used, the absorption always proceeded slowly and with well-marked anatomical changes.

The animals were killed at intervals of from a few days to six or more weeks after the operation. The eyes were fixed in corrosive sublimate and the piece of cornea and iris, including the site of the foreign body, embedded in paraffin, cut serially, fixed on the slide and stained with hematoxylin and eosin, van Gieson's stain, etc.

THE HISTOLOGICAL EXAMINATION.

Comparatively slight attention was given the study of the early changes. Suffice it to say that the emigration of leucocytes from the vessels of the iris took place to a limited extent only, at least in the cases in which bits of solid blood serum are concerned. The leucocytes present were of the polymorphonuclear variety, and they appeared to become loaded early with granules of serum, after which some of them returned to the iris, in which a few collections of such cells were found. In the later

stages of the resorptive process leucocytes were not observed.

The new cells produced come almost wholly, it would seem, from the layer of polyhedral cells clothing the inner surface of the posterior elastic lamina (Descemet's membrane) and the anterior surface of the iris. The posterior lamina itself generally remains quite intact. The new cells, which are round, oval or polyhedral, accumulate around the foreign body and penetrate into its interior, generally breaking it up, so that there is formed a mass of cells which adheres to the elastic layer and encloses the granular detritus of the coagulated serum. Most of the cells take up granules into the interior of their cytoplasm, often to such an extent that the nucleus and the entire cell appear as if buried beneath the granular mass. The serum granules, whether free or intracellular, are easily recognizable because of their brownish or golden yellow color (derivatives of hæmoglobin pigment).

During this time there are formed a small number of multinucleated giant cells or plasmodial masses, which appear, as far as these observations show, to result from fusion of many small cells. These giant cells do not differ in form and in their general characteristics from those ordinarily observed in connection with the absorption of sterile foreign bodies elsewhere. Their size and the number of nuclei, which are scattered uniformly throughout the body of the cell, vary considerably. In the earlier stages the cells are loaded with serum granules and are of circular outline; later when the foreign body has been largely removed the giant cells become oval or oblong, due, it would seem, to the pressure of the new fibers that in the meantime have formed around them.

The granules of solid blood serum without and within the cells gradually disappear, largely, it would seem, by means of a process of intracellular digestion or solution;

in some of the giant cells as well as in the smaller cells occur vacuoles in the cytoplasm containing granules; some of the serum, but not much, is also transported into the iris by leucocytes.

Simultaneously with the destruction or removal of the foreign granules the uninuclear and multinuclear cells begin to show further and progressive changes that ultimately lead to the formation of a layer of tissue which much resembles the cornea in structure. These changes begin first and are farthest advanced at the periphery of the cell mass, extending little by little throughout the central part.

The changes consists in the production of a fibrillated intercellular substance, or stroma, while at the same time the cells become spindle-shaped and elongated, the nuclei more slender and fusiform. All the stages in this transformation of embryonal cells to mature tissue, during which the granules of serum are destroyed, can be quite readily traced. In the later stages the fibrillæ of the new stroma are gathered together into interlacing bundles of considerable thickness, the general course parallel to the corneal lamellæ, from which they are separated by the intact posterior elastic lamina. While the course and arrangement of these new fibers are identical with those of the cornea, yet the new lamellæ are not so thick and densely interwoven as those in the cornea and they stain more deeply with eosin. This new tissue, the free surface of which becomes covered by a distinct endothelial lining, may finally appear as a mere rounded or pyramidal-shaped thickening on the posterior surface of Descemet's membrane, or it may unite the cornea with the iris, especially if the foreign body found a resting place in the irido-corneal angle.

Lying in the spaces of the new tissue, sometimes apparently upon its fibers, are small cells like connective tissue cells, occasionally cells containing granules as well as free heaps of serum detritus and, in the stages not too

far advanced, multinucleated giant cells in the process of separation into uninuclear cells.

It has already been stated that in the earlier stages the giant cells are more or less circular and the margins smooth and even. As the fibrillated stroma forms about them they may in many cases become oval and even distinctly oblong, this occurring simultaneously with the disappearance of the serum, the long diameter corresponding to the direction of the fibers of the stroma. At this time they are usually entirely, or almost entirely, free from granules of serum; occasionally there may be vacuoles containing granules in the protoplasm. It should be emphasized that there are no signs of degeneration in the giant cells; the cytoplasm is reddish when stained by eosin and sometimes finely granular, but often it appears dense and homogeneous; the nuclei stain perfectly, and in one instance a dividing nucleus in the daughter star stage was observed in a giant cell.

As the serum disappears more or less distinct lines of cleavage become visible in the giant cells, at first most marked at the periphery; the margin is not smooth and even, but is fringed by the spindle-shaped projections of partly separated cells which seem to have a tendency to arrange themselves parallel with the fibers of the stroma. Single uninuclear cells which are exactly similar to these partly detached masses are occasionally found about the giant cells. In some giant cells, especially those encountered in the older and firmer parts, there are lines of separation throughout their entire extent, lines running in such a manner that single nuclei surrounded by more or less cytoplasm are completely or incompletely mapped out; it is noteworthy that in these cells the lines of cleavage map out more or less distinctly spindle-shaped cells, the long axes of which correspond in direction to the fibers of the stroma. Occasionally the lines separating a nucleated mass are so broad and well marked that it appears as though a distinct

cell were lying in a vacuole; the cytoplasm of such giant cells especially takes place more slowly, and the impression is received that this may all be caused by the pressure exerted upon the giant cell by the fibrillated stroma in which it is enclosed, or that the cytoplasm is being transformed into the same sort of substance as the fibers of the stroma. The separation of small cells nevertheless continues, because in the older tissue are found small giant cells containing a few—three or four—nuclei and embedded in a dense capsule of nucleated tissue, without any traceable evidences of nuclear disintegration or of destruction of the giant cells by phagocytes.

When the serum is absorbed rapidly and the giant cells lie in the broad and loose meshes of the new-formed fibrillated tissue, the lines of cleavage may be quite complete, so that single nuclei, surrounded by an irregularly shaped bit of cytoplasm, are split off and imperfect giant cells result, which are surrounded by uninuclear small cells that fit the depressions and elevations on the remnant of the subdividing plasmodial mass. Uninuclear cells thus produced present no signs of necrobiosis and can be traced by means of transition stages into the elongated and flattened cells above described as lying in the new-formed tissue. Nuclear and protoplasmic detritus, as well as evidences of immigration of small cells or leucocytes into giant cells, are not to be observed.

CONCLUSION.

The conclusion seems warranted that the giant cells formed in the absorption of coagulated blood serum inserted into the anterior chamber of the rabbit's eye subdivide again into uninuclear small cells that take part with other new-formed cells derived from the lining of this space to form a densely fibrillated mass of tissue that resembles quite closely the cornea in its structure.

This demonstration materially strengthens the opinion expressed by the writer in his previously mentioned article that the giant cells in healing non-degener-

ated tuberculous tissue may separate into small living cells, and that the giant cells of tuberculosis are not necrobiotic elements from the very moment and from the very mode of their formation, as has been the general teaching, especially in Germany.

April 11, 1898.

TUBERCULOSIS IN DOGS.

WALTER H. SHELDON.

It is admitted that rabbits, guinea-pigs, cats, and field-mice are susceptible to the bacilli of human tuberculosis. There is a difference of opinion in regard to the extent of the prevalence of this disease among dogs and their susceptibility to it.

Ziegler states that it occurs in dogs exceptionally. Abbott says that "white mice, dogs, and rats possess immunity against the disease;" Osler that "dogs and cats are not prone to the disease;" Carl Günther says that "white mice, rats, hens, and canary-birds are less susceptible to infection than guinea-pigs, cats, and field-mice." Fränkel and Sternberg do not mention tuberculosis in dogs.

Comparatively little is definitely known about the subject, and it becomes a matter of interest and practical value when cases of tuberculosis can be proven.

Study of the subject in veterinary journals and books treating particularly of diseases in dogs shows, however, that it is more common than is generally supposed. It is important for one to know that the dog, the friend of man, is far from being immune to this disease. In these days, when dogs are fondled by children and are allowed to live to an advanced age for association's sake,

there is frequently real danger of the spread of this disease through them.

To indicate how frequently tuberculosis occurs in dogs, it may be mentioned that a request to the Bureau of Animal Industry in Washington for references upon this subject was answered by a list of thirty-four articles, mostly in German and French. This was only a partial list, but over one hunderd and fifty cases of tuberculosis were cited, all of which were authenticated by the finding of the bacilli.

Most of these articles are of recent date, and the researches have been carried on in a comparatively small number of laboratories. The following is taken from an article in *Monatshefte für Prakt. Thierheilk.*, 1895, by Froener, entitled "Dreizehn weitere Fälle von Tuberculose beim Hunde." There have been recently published, mostly abroad, one hundred cases of alleged tuberculosis in the dog. Cadiot alone has reported more than forty, Jensen twenty-eight, and Eber eleven; Froener observed twenty-seven during the year 1894, and in his last article announces a series of thirteen more. Froener writes: "In these autopsies the lesions varied according to the age and the localization of the disease, the organs of the thorax being those most frequently affected. In the thirteen cases the lesions occupied the lungs and pleura eleven times, the river ten times, the bronchi and ganglia of the mediastinum six times, the pericardium five times, the kidneys three times, and the spleen once; all the organs were involved in one case." He gives a summary of the general pathological appearance of the different organs.

J. H. Steele, in his book on "Diseases of the Dog," published in 1888, writes: "There occur in the dog some disorders of the lungs, mesenteric glands, and other parts of the body, which have all the appearance of tuberculosis, and yet we are not aware of any distinct evidence having been brought forward that true con-

sumption, due to the tubercular bacilli, is ever found in the dog."

A number of cases are cited in the literature where the dog acquired tuberculosis from man. In Friedberger and Fröhner's "Pathology and Therapeutics of the Domestic Animals" we read: "In the dog tuberculosis is not so rare as has been admitted. It is probable that in a majority of cases it is of human origin; the dog contracts it by licking virulent expectorations. We have gathered a few personal observations which testify in favor in this theory. In one case, three dogs belonging to the same owner became infected and died of generalized tuberculosis. The symptoms are those of chronic pulmonary disease with emaciation. In two dogs we have been able to recognize the bacillus in the discharge. In one dog striking improvement resulted from prolonged inhalations of creolin, one-half per cent.

In the *Veterinary Journal* for June, 1899, Austin Peters cites an interesting case of tuberculosis in a dog: "A young dog in the habit of eating the sputa coughed up by the dog's mistress, who had consumption, had seemingly a bad cold, but as it was suspected that the dog might have tuberculosis and might communicate it to the children, it was killed and an autopsy held. Phthisis of both lungs was found, and a large abscess in the posterior lobe of the left lung. Smears were made from walls of the abscess and many tubercle bacilli were found."

M. Neyrand, in *Recueil de Médecine Véterinaire,* 1894, tells of a setter six years old, emaciated and with no appetite. The owner was a consumptive, and the dog had been seen to eat the sputa of his master. The dog was put under treatment, but after eight months was deemed incurable and killed. Autopsy revealed tuberculosis, and many tubercle bacilli were found.

The case which I wish to add to this already large list was that of a dog, about eight years of age, which had

been sick for two years. There was increasing emaciation, frequently attacks of ascites, and languor. My fellow student, Mr. O. A. Dahms, obtained possession of the dog and killed it. The pericardial sac was distended with fluid, the pericardium much thickened, and with the epicardium was covered with gray and yellow nodules of various sizes. (The heart is now in the museum of the Pathological Laboratory of Rush Medical College). The lungs were apparently normal. The peribronchial glands were enlarged and the peritoneum adhered in many places; the liver was sparsely covered with grayish nodules. The stomach and the pancreas were apparently normal. Numerous yellowish nodules as large as a pea were present on the spleen. The kidneys showed a limited number of similar nodules.

A piece of a pericardial nodule was inserted into the abdomen of a rabbit.

Sections were made of the liver, pericardium, kidney, and heart of the dog. In the kidneys there was atrophy and considerable necrosis of the epithelial cells lining the convoluted tubules. In the lumen of the tubules there was an accumulation of necrotic material, which stained with eosin and was homogeneous in structure. Many of the blood-vessels were hyperemic and there was considerable proliferation of connective tissue. The sections of the heart showed circumscribed masses, made up of epitheloid and spindle-shaped cells. No giant cells were found, and there was much fibrous tissue.

Sections of the heart, pericardium, and liver containing tubercles were stained by the Ziehl-Nielson-Gabbet method for the bacilli, and large numbers of them were found. Considerable search was necessary to find them in the sections made from the pericardium.

The rabbit which had been inoculated gave birth to young a few days after the inoculation. It soon began to grow thin; the wound in the skin healed, but some en-

largement remained. The rabbit was killed six weeks after inoculation.

No remains of the tubercle which had been inserted could be found. The mass at the site of inoculation was composed of little nodules the size of a pin-head, and the whole mass was about half an inch in diameter and an inch in thickness. The kidneys, liver, spleen, heart, pericardium, and lymphatics were normal. The lungs contained numerous small foci from the size of a pin-head to three times this size.

Sections made of the subperitoneal tubercles and of the miliary tubercles in the lungs showed tubercle bacilli in large numbers. A microscopical examination showed typical tubercles with very few giant cells. From this review and from the study of our case we may deduce the following:

1. Tuberculosis, probably of the mammalian type, is not as rare in dogs as is ordinarily supposed.

2. Dogs are prone to become infected by licking up the sputum of tuberculous patients; the location of the primary point of lodgment in such cases is not yet clear.

3. As shown in the case here described, the gross lesions of tuberculosis in the dog resemble those of the subacute and chronic forms in man, especially when the pericardium is involved. The absence of caseation and the absence in this case of giant cells are, however, points of deviation from the common type of human tuberculosis.

4. Dogs with cough, emaciation, or other symptoms that may be due to tuberculosis, should as a prophylactic measure be killed. They may spread the disease, especially if the lungs are involved.

June 17, 1898.

INFECTION WITH THE BACILLUS PYOCYANEUS, WITH REPORT OF A CASE.

DANIEL N. EISENDRATH.

We have been accustomed to look upon the bacillus pyocyaneus as rather a curiosity in medicine, having been found in the atmospheric air, upon the skin, in the saliva, sputum and sweat of the human organism. We are all familiar with the phenomenon of green pus and the fact that it is due to this bacillus, but do not associate this microbe with the other pyogenic organisms in the etiology of general sepsis. Nevertheless, evidence is gradually accumulating that we must regard the bacillus pyocyaneus in a far more serious light than we have done in the past. Despite the assertions of individual writers like Schimmelbusch[1] and Shurmeyer[2], that the bacillus pyocyaneus has no general pathogenic action, recent literature contains a number of interesting and careful observations made by reliable investigators to show that it is more frequently present as the only cause of general pathological conditions in the human organism than has been generally supposed.

Gessard[3] in 1882 found a short, very motile organism in green pus. It grew on gelatin, agar, and potato, generating on the two former a light-green coloring matter, upon the last named a brownish pigment. In 1887 Ernst[4] described a second variety, which differs only by giving the so-called chameleon reaction—*i. e.,* upon touching a nut-brown potato culture with a needle it becomes dark brown. The bacterial cells themselves are colorless, but in nutrient media two pigments are formed, pyocyanin and pyoxanthose. Injected into animals it produces either an acute infection with diarrhea, convulsions, and cachexia, with death in twenty-four hours, or causes paralysis in chronic cases, to which Charrin[5] has called attention. An interesting fact is that an an-

tagonism exists between the anthrax bacillus and bacillus pyocyaneus. The former does not develop as rapidly in cultures, nor kill animals when inoculated with the bacillus pyocyaneus. The toxins injected into animals, as shown by Charrin[6], cause rise of temperature and a group of nervous symptoms which he terms spinal epilepsy, namely, a spastic condition of the hind limbs with muscular atrophy, disturbances of sensibility, arthritis, and ulcerations of skin. An exactly similar condition occurs in man, as shown by Burot[7]. He reported the case of a woman, forty-four years of age, who had contracted a severe form of malaria. During this illness she had an acute coryza. Whitish areas on the skin appeared over various parts of the body, followed by extensive ulcerations. There were also present muscular atrophies, contractures, especially of the right arm. From time to time hemorrhagic spots would appear, which would ulcerate. In all of the ulcerations a pure culture of the bacillus pyocyaneus was found. Later on there was a temperature varying from 99° to 103°. Burot believes that the source of infection was a cat which was covered with ulcerations.

In the discussion which followed this report Charrin said there were two forms of pyocyaneus infection, a general septic and a cutaneous, and this seems to be the opinion of most writers on this subject. Laborde and Charrin[8] injected rabbits with cultures of the bacillus pyocyaneus and found some remarkable nervous symptoms. There was drooping of the head, the neck, and later of the entire body, with rotation to the left. Then paraplegia appeared, extreme emaciation, nystagmus, and hemianesthesia. These symptoms show the profound influence of the toxins upon the nervous system. In their later experiments[9] they particularly call attention to the fact that according to the dose of the toxin they could produce neuritis, myelitis, hemorrhages of the hemispheres, of the peduncles, and of the medulla. Two

clinical forms above spoken of may either occur separately or, as is frequently the case, combined, especially in children. Neumann[10] was one of the first to call attention to this form of infection. He reported two cases of infants who showed petechiæ on the skin of the breast and thighs, with hemorrhages from the intestines, in which the bacillus pyocyaneus was obtained in pure culture from the spleen, liver, kidneys, blood, and intestines. In both there were found post-mortem numerous small hemorrhages in the small and large intestines. A number of similar observations have been made by Williams and Cameron[11], which it will repay to quote in detail.

In the first case, a baby was nursed by its mother until it was twenty-two weeks old. It then became restless and lost in weight, with slight temperature from 99° to 100°, abdominal pain and tenderness, but no tympanites. At the end of five weeks of such indefinite symptoms a group of purple papules appeared upon the abdomen, followed during a fortnight by numerous similar papules with greenish stools and diarrhea. In two or three weeks the depression became extreme. The child would not move its limbs. The legs were flexed on thighs and these on abdomen, and any attempt to straighten them was followed by a moan and a return to the former position (a form of spastic paralysis). Shortly after there was a profuse epistaxis and many subcutaneous hemorrhages appeared. There was also a purulent discharge from the ear. The child became comatose and died. In sections made from the kidneys, spleen and liver, the capillaries were found to be blocked with emboli formed by bacilli, with hemorrhagic areas in the kidneys. In the liver, spleen and kidneys pure cultures of the bacillus pyocyaneus alone were found. There were none in the intestine. The cultures made from the papules remained sterile, probably on account of the bichloride with which the skin had been washed.

The second child had been nursed by its mother for two months; then while artificial foods were used, there was a steady loss in weight with discharge from both ears. The stools were green, very frequent, and of very offensive odor. There were no purpuric spots or hemorrhage, but marked lividity of the body. The child died shortly after. The spleen, liver and kidney contained pure cultures of the bacillus pyocyaneus. The ears in this latter case might be a possible source of infection, as shown by Bloxall[13], who found the bacillus pyocyaneus in an ear discharge complicating scarlatina.

In a third case, reported by the same authors[12], similar bluish papules appeared upon the abdomen, followed by spots elsewhere. There was a discharge from the right ear, slight cyanosis, and rigidity of muscles of the legs. In this case the bacillus pyocyaneus was found in pure cultures in the blue papules on the skin.

Ehlers[14] reports two cases occurring in children in which there was fever, diarrhea, albuminuria, resembling a typhoid clinically. Upon the eleventh day a bullous eruption appeared, and in these the bacillus pyocyaneus was found in pure culture. One died, and in the blood post-mortem the same organism was found in pure culture.

Finkelstein[15] observed three cases of marasmus in infants in whom upon touching the skin in the last days before death hemorrhagic spots would appear. In all of these spots he constantly found the bacillus pyocyaneus, and believes that it had a direct etiologic relation.

Kossel[16] adds to these cases of general infection three interesting ones. In one child four weeks old there was present diarrhea, greenish vomiting, anorexia, and extreme weakness. The bacillus pyocyaneus was found in very large numbers in the stools, crowding out the ordinary intestinal bacteria. The temperature rose to 104°, death occurring shortly after. The autopsy showed

pus in the middle ear and on right side of nose. In this pus, as well as in the mucus covering the larynx and trachea, there were found pure cultures of the bacillus pyocyaneus. It was also present in very large numbers in the stomach and small intestine. Another important case was that of a marantic infant with fine moist râles over both lungs and gradual decrease in weight. Death occurred soon after admission. The pia-arachnoid showed a marked serous exudate. Over the base of the cerebellum there was a large purulent exudate. Both tympanic cavities contained pus. The bacillus pyocyaneus was found pure in the meningeal exudate and in the blood taken from the heart. In the ear it was found with diplococcus Fräenkel.

Triboulet[17] reports a case of a child, aged ten months, with diarrhea, fever (104°), and an impetigo accompanied by ulcerations, which contained almost a pure culture of the bacillus pyocyaneus. Post-mortem this organism was found in the blood taken from the heart, and in the liver and kidney.

As an example of a general disease in an adult caused by the bacillus pyocyaneus, the following case reported by Kranhals[18] may be quoted: A man, 40 years of age, had been operated upon for empyema. Suddenly, after one month of undisturbed healing, the patient had high fever, accompanied by diarrhea. The wound looked well. After several weeks of continued high fever the patient died. The post-mortem showed a purulent mediastinitis, entero-colitis, enlarged spleen, and pericardial exudate.[4] In the three first named, a pure culture of the bacillus pyocyaneus alone was found.

Jadkewitsch[19] reported an interesting case in which in a patient with chronic eczema of both lower imbs, bluish-green pus formation occurred three times in ten years, accompanied by emaciation, prostration, and once diarrhea. There was also distinct anesthesia and paresis not only in the limbs, but also of the tongue and lips.

During the third attack he cultivated the bacillus pyocyaneus from the urine. The symptoms in this case closely resembled the experimental picture obtained by the injection of the bacillus pyocyaneus toxin in animals.

In a case of Oettinger's[20] a young man, 19 years old, presented typhoidal symptoms for nineteen days—violent headache, vertigo, ringing of ears, constipation. On account of a suppurating index-finger the diagnosis was at first reversed. It was thought possible that the case might be one of general infection from a local cause. The continuous type of fever remained for nineteen days. The patient seemed to be convalescing from an attack of typhoid, when suddenly the temperature rose, and all of the other symptoms reappeared, accompanied by bullous eruption, the bullæ filled with serous, bloody fluid, from which the bacillus pyocyaneus alone was found in pure culture. Here the invasion of the system with the bacillus pyocyaneus was probably a secondary infection.

Karlinsky[21] reports the case of a laborer 48 years of age who was operated upon on account of a phlegmon of the forearm. The staphylococcus aureus and bacillus pyocyaneus were found in the pus. Upon the seventh day the temperature rose suddenly to 105°. Upon the ninth day small red papules appeared on the body, which gradually became dark blue, then vesicular. The serum which they contained showed a pure culture of the bacillus pyocyaneus alone. The vesicles changed soon to ulcerations. On the thirteenth day the patient began to vomit frequently, and to have diarrhea. The spleen was much enlarged. He became comatose, and died. At the autopsy inoculations made from the spleen, blood, swollen and slightly necrotic Peyer's patches revealed cultures of the bacillus pyocyaneus alone.

Barker[22] published eleven cases examined post-mortem at the Johns Hopkins Hospital. The most interesting of these is one of a negro, aged 40, with extensive skin

disease resembling acute exfoliative dermatitis, who died of a complicating bronchopneumonia. The bacillus pyocyaneus was found in the lung and cutaneous lesions.

Lartigau[23] has recently published a case in which the diagnosis of a general pyocyaneus infection was made post-mortem, greatly resembling my case. His case is as follows: An unmarried woman, 19 years of age, was suddenly seized with general abdominal pains, fever, chills, nausea and vomiting. The symptoms subsided, and recurred at a following menstruation. She was admitted with a temperature of 102.4°. Abdomen markedly tender over right pelvic region, where a large indefinite fluctuating mass could be felt. An incision was made, and pus evacuated. On the second day after the operation there was marked tympanites, apathy, diarrhea, and a fine papular rash over the trunk and limbs. Temperature ranged between 101° and 103°, death occurring on the fifth day. At the autopsy the following was found: A purulent peritonitis, pyosalpinx, a circumscribed collection of greenish pus in the cul-de-sac, an acute hemorrhagic enteritis, with superficial ulceration of the small and large intestine, and an acute splenic tumor. Cultures were taken from the heart's blood, liver, spleen, lungs, general peritoneal cavity, Douglas' pouch, kidneys, and intestinal ulcers. The organism common to all was the bacillus pyocyaneus:

The case which I desire to add to those above given is as follows:

Mrs. M. R——, aged 24 years, entered the Michael Reese Hospital on August 22, 1898, under the care of Dr. Henry Banga, to whom I am indebted for the permission to publish this case. Her family history was negative. She had always been in good health prior to her marriage, one and one-half years ago. Her menstruation had begun at the age of 14, and was normal. Soon after her marriage she noticed a discharge, and began to have pain over both iliac regions at the time of menstruation, at times very severe. She had a whitish discharge from the vagina, and five months before admission she

was taken suddenly ill with chills, nausea, vomiting, and headache. These chills recurred at irregular intervals, and she had high fever during this period. These symptoms were at first accompanied by pain in the pelvis, followed by pain all over the abdomen, with tympanites. This was diagnosed as peritonitis by her physician. During the entire attack she had diarrhea. The temperature, headache and abdominal symptoms had gradually subsided. There had been no nervous symptoms, motor or sensory. For a short time there had been an extensive pustular eruption over the breast, back, and arms. During her first four weeks in the hospital her temperature varied from 99° to 100°. There was diarrhea, which it was impossible to control. The urine contained hyaline and granular casts. The abdomen was flat.

On Sept. 20, 1898, an abdominal section was made by Dr Banga. The coils of intestines were found universally adherent. The ovary on the left side was enlarged to the size of a clenched fist, and contained pus. This was aspirated and the ovary removed. The same condition existed upon the opposite side, and the ovary and tube were removed. Following the operation to the present time the patient has had from five to ten bowel movements daily. The pus was sent to the laboratory of the hospital, and inoculated upon all of the ordinary media. Upon all of these it grew in the manner characteristic of the bacillus pyocyaneus. The cultures were pure and contained no other organism.

The further investigations to confirm the identity of this bacillus gave all of the typical reactions, and growths characteristic of this organism. The case of Lartigau above spoken of, and one of Baker's[22], as well as this case, show that the bacillus pyocyaneus can give rise to an infection of the adnexa, with secondary peritonitis and a general pyocyanic infection.

The bacillus pyocyaneus has been frequently found as the cause of other local infections without such general symptoms as those just mentioned. It has been found in pure cultures alone in suppurative middle-ear disease by Martha,[24] Maggior and Gradenigo,[25] Babes,[26] Kossel,[27] and others; in bronchitis and bronchopneumonia by Lartigau, Barker, Mornier, and Harbitz.[28] Blumer[29] found it in pure culture in a case of angina. In esophageal, gastric and enteric lesions it has been found by Barker and other investigators; in abscess of the liver

by Kraus and Pasquale.[30] Of the serous membranes an interesting case of pericarditis with effusion has been reported by Ernst[31], and also one in the series observed by Barker. In the endocardium the latter found it in pure culture in one case; in the peritoneum in the cases detailed above; in the pleura by Lartigau; in the genito-urinary tract it has been observed by Motz;[32] in a case of cystitis in a child by Le Noer;[33] by Barker in ureteritis and pyelonephritis, associated with the bacillus coli communis.

We thus see that the bacillus pyocyaneus is by no means the harmless organism which we have supposed it to be. To sum up, we find that it may cause either a local or general infection, the clinical symptoms of the former depending upon the organ or tissue involved, but nevertheless as constant as those resulting from infection with the ordinary pyogenic microbes. The symptoms of the general infection are well shown in the case I have reported, viz., headache, fever, chill, vomiting, diarrhea (both of the latter evidence of the specific lesions in the alimentary tract), rapid pulse. In children the stools are of a greenish color and the disease has a longer course. The more chronic the infection, the more prominent do the nervous symptoms become both in children and adults. This is confirmed by the cases quoted, and by the experiments of Charrin on animals. According to Cameron and Williams, the characteristic symptoms in children are emaciation, diarrhea, fever (slight), albuminuria, purplish or bluish papular eruption, nervous symptoms (spastic paralysis, etc.). In the more acute cases the pathological lesions are vasomotor disturbances, focal necrosis, hemorrhages into the skin, serous and mucous membranes, lesions in the parenchyma of the heart, liver, spleen, and kidneys; the intestinal lesions, acute or chronic inflammation, with ulceration, especially of the small intestine. In the case I have reported the atrium of infection is unknown

—whether through the genital tract is still an open question. In many cases the atria are the ear, suppurating wounds as lately shown by Lartigau,[34] gastro-intestinal and genito-urinary tracts. However, there can no longer be any question that acute and chronic, general and local pyocyanic infections occur in the human organism. The treatment with antipyocyanic serum, which for pyocyaneus infection Bouchard showed was possible before the diphtheria serum was discovered, is the only one to be suggested.

October 10, 1898.

BIBLIOGRAPHY.

1. Volkmann's Sammlung Klin. Vorträge, No. 62.
2. Zeitschrift für Hygiene, vol. xx, p. 281.
3. Comptes Rend. de la Soc. de Biol., 18, tome 94, 1882.
4. Zeitschrift für Hygiene, 1887, Band 2.
5. Comptes Rend. de la Soc. de Biol., 1890, p. 41; La Maladie Pyocyanique, Paris, 1889. Traite de Médicine, Bouchard, 1892, tome 1.
6. Comptes Rend. de la Soc. de Biol., p. 373, 1895.
7. Comptes Rend. de la Soc. de Biol., June 4, 1898.
8. Comptes Rend. de la Soc. de Biol., 1890, p. 652.
9. Comptes Rend. de la Soc de Biol., 1896, p. 32.
10. Archiv für Kinderheilkunde, 1891, xii and xiii.
11. Journal of Pathology and Bacteriology, 1896, p. 344.
12. Montreal Medical Journal, March, 1896.
13. British Medical Journal, 1894, p. 116, vol. ii.
14. Comptes Rend. de la Soc. de Biol., 1890, p. 496.
15. Charité Annalen, 1896, p. 346.
16. Zeitschrift für Hygiene, 1894, vol. xvi.
17. Comptes Rend. de la Soc. de Biol., Oct. 22, 1897.
18. Deut. Zeitschrift für Chirurgie, p. 185, 1893.
19. Baumgarten's Jahresbericht, 1890.
20. La Semaine Médicale, 1890, p. 385.
21. Prager Medicinische Wochenschrift, 1891, No. 20.
22. Journal of the American Medical Association, July 31, 1897.
23. Philadelphia Medical Journal, Sept. 17, 1898.
24. Arch. de Méd. Exper., 1892, p. 130.
25. Annales de l'Institut Pasteur, tome v.
26. Les Bacteries, p. 486.
27. Op. cit.
28. Baumgarten's Jahresbericht, 1895.
29. Johns Hopkins Hospital Bulletin, 1895.
30. Cited by Barker.
31. American Journal of the Medical Sciences, p. 396, 1894.
32. Comptes Rend., 1896, p. 128.
33. Comptes Rend., 1896, p. 71.
34. Op. cit.

THE PRODUCTION OF FLUORESCENT PIGMENT BY BACTERIA.

EDWIN O. JORDAN.

A considerable number of different "species" of bacteria have been described as endowed with the property of forming a blue green fluorescent pigment in suitable media. I append a list, perhaps not complete, of the various "fluorescent bacteria" already discovered.

It is not at all likely that the fifty names bestowed upon these cultures represent as many totally distinct micro-organisms, and in some cases it is practically certain that the same bacterium masquerades under several different titles.

The experiments recorded in the present paper embody a series of attempts to discover the conditions under which fluorescence is produced, and especially the nature and amount of the chemical substances essential to the formation of the fluorescing body.

I have chosen for this purpose six different cultures[1]. Four of these do not liquefy gelatin and were sent to me from Kral's Laboratorium under the names B. fluorescens albus, B. fluorescens tenuis, B. fluorescens mesentericus, and B. fluorescens putridus. The two others liquefy gelatin; one of them was sent by Kral with the name B. viridans, and the second was isolated by me from the water of Lake Michigan and identified as B. fluorescens liquefaciens (description by Kruse in Flügge's Die Mikro-organismen 2:292).

1. B. FL. ALBUS.—A bacillus was first described under this name by Zimmermann, who found it in the Döbeln water supply.[2] The culture bearing this name which I have employed agrees closely with Zimmermann's description. The bacilli are small (0.6 by 1-2 microns) with rounded ends, and occur both singly and in short chains: they are actively motile. Upon gelatin plates the colonies spread out into a thallus-like

expansion and the surrounding medium assumes first a blue-green tint. The growth on agar is elevated and translucent white, and a green fluorescence is imparted to the medium. The growth on potato is luxuriant, and has a rich chocolate-brown color. Milk is not coagulated, no indol is formed, and nitrate is not reduced. In the fermentation-tube no gas is produced, but the broth is rendered strongly acid. At 37.5 C. a good growth takes place upon agar, but no pigment is produced at this temperature. A perceptible amount of pigment is formed at 33 C.

2. B. FL. TENUIS.—Described by Zimmermann[3] as a distinct species. Found also by Dittrich[4] and regarded by him likewise as a distinct species. Kruse,[5] however, considers this organism as merely a variety of B. fluorescens non-liquefaciens. My own culture bearing the name of B. fluorescens tenuis agrees very closely with B. fl. albus. The chief points of difference are *a*, its failure to grow at all at 37.5 C.; *b*, its ability to produce a small amount of indol in sugar-free broth.

The fine, delicate leaf-like growth in streak-cultures, upon which Zimmermann chiefly bases his separation of this "species" from B. fl. albus, was noticed sometimes in my culture, but was not constant.

3. B. FL. MESENTERICUS.—Described by Tartaroff.[9] I have not been able to see the original description. The culture sent me under this name resembles B. fl. albus very closely. There are slight but inconstant differences in the growth of the two cultures upon gelatin, agar, and potato. The growth at 37.5 C. is much less profuse than with B. fl. albus and no pigment is formed when the culture is kept at 33 C. Milk is slightly digested and acquires a feebly acid reaction.

4. B. FL. PUTRIDUS.—Described in Flügge's Die Mikroorganismen, 2d edition, p. 288; cf. also the 3d edition, 2:292. My own culture bearing this name agrees in most respects with B. fl. albus. The chief differences are *a*, much scantier growth at 37.5 C.; *b*, less rapid growth on all media; *c*, a dry, thin growth on potato, more restricted and duller than that of B. fl. albus; *d*, a much more decided green tinge imparted to milk.

These differences, although slight, have been constant during some ten months of observation. I have not been able to distinguish any difference between the character or intensity of the odor given off by this species and that observed in the three cultures previously described.

5. B. VIRIDANS.—A micro-organism was first described under this name by Symmers.[7] Zimmermann[8] also described a form found in polluted water which he pronounces wholly identical with a culture of B. viridans (Symmers), obtained from Kral.

My own culture bearing this name was sent me from Kral's collection.

The bacilli vary considerably in dimensions when grown on different media. They are short and quite slender in broth cultures, longer and plumper on potatoes. On the latter medium they average about 0.8-0.9 microns by 2.5-3 microns. They occur usually singly or in pairs when grown in broth, and are non-motile. They stain with the ordinary aniline dyes, but not so readily as with carbol-fuchsin or Löffler's methylene blue. They do not retain the stain by Gram's method. Gelatin is liquefied very rapidly, the growth in a stabculture occurring at the upper part of the inoculation line and giving rise to a saucer-shaped depression. The growth in agar streak-culture is gray, thin, fairly spreading and with serrated edges. The medium is speedily colored a fine blue-green which in seven days has changed to a dark Nile-green. The growth on potato is luxuriant, at first dry and of a tan-color, but later becoming dark and slimy. Milk is curdled with acid reaction, and the whey assumes a decided green color. No indol is formed, and nitrate is not reduced. In the fermentation tube no gas is produced in glucose bouillon but the medium becomes strongly acid. At 37.5 C. a very scanty growth occurs, but no pigment is produced.

Zimmermann[9] classifies this organism as one that produces green, but not fluorescent pigment. I have not been able to remark the existence of any such difference between my culture of B. viridans and the other organisms I have studied; fluorescence is manifest in all.

6. B. FL. LIQUEFACIENS.—A germ isolated by me from the water of Lake Michigan. I have given it the above name, since the culture agrees with the description of the species by Kruse.[10] The chief differences between this culture and that of B. viridans are the following: *a*, no growth at all occurs at 37.5 C.; *b*, growth in gelatin stab-cultures is more rapid than that of B. viridans under the same conditions, but pigment is less abundantly produced; *c*, the bacilli are actively motile; *d*, growth on potato is from the outset moist and slimy; *e*, nitrate is readily reduced to nitrite.

It is evident from these descriptions that the existing differences between some of the cultures I have employed are hardly to be regarded as specific, whatever may have been the case with the type micro-organisms when first isolated. I shall for convenience, however, refer to the cultures by the names they bear just as if they were so many distinct "species."

The methods employed have been selected with a view

to obtaining constancy and uniformity of conditions. Owing to the familiar fact that the different commercial peptones vary widely in chemical composition and nutritive value, and since Gessard[11] and Lepierre[12] have definitely proved that the production of fluorescence by certain bacteria is profoundly affected by the nature of the peptone used, I have carried out my investigations with the aid of simple solutions of chemical compounds whose molecular composition and arrangement are more accurately known. The nitrogenous basis of these nutrient media has consisted of asparagin or ammonium salts, and to these have been added other substances according to the nature of the experiment. The utmost care has been taken to obtain chemicals of strict purity, since a mere trace of foreign substance is in some cases sufficient to vitiate the result.

In all of my solutions I have employed water redistilled in glass. The various flasks and test-tubes in my experiments have been thoroughly cleansed with chromic acid cleaning mixture which has been very carefully washed out and the vessels finally rinsed in distilled water. A suitable quantity (usually 7-8 c.c.) of the nutrient solution has been placed in thin-walled test-tubes and sterilized in the steam-bath by the discontinuous method. Prolonged heating and the use of the autoclave have been avoided as they have been found to affect the constitution of some of the media.

Inoculation of the media has usually been made from vigorous agar growths about three to five days old, but I have also often used for this purpose fluid media in which abundant production of pigment had occurred, e. g., an asparagin-phosphate-sulfate solution, but without noting any difference in the outcome.

The cultures have always been kept in the dark and at the room-temperature, 18-20°C., except when specified otherwise.

The most extended contribution to our knowledge of

the fluorescent bacteria, with the exception of Gessard's classic papers upon B. pyocyaneus, is contained in a paper by Thumm[13]. My own observations conflict with Thumm's at some points, while the conclusions I am compelled to draw from my results are, in important respects, so at variance with his that I do not hesitate to reopen the whole question and to present the record of my experiments in some detail.

INFLUENCE OF THE CHEMICAL COMPOSITION OF THE MEDIUM.

In 0.2 per cent. pure asparagin solutions a very slight turbidity occurs, but no trace of color. If 0.1 or 0.5 per cent. of chlorid (sodium, calcium, magnesium, or potassium) be added to the asparagin solution, the turbidity is slightly increased, but no pigment is formed. Sulfates (sodium, magnesium, or potassium) in the same proportion aid the growth more than chlorids, but no color appears. Pure phosphates (sodium, magnesium, or potassium) are yet more favorable to growth, but fluorescent pigment still fails to develop. I must at this point lay stress upon the importance of obtaining chemically pure phosphates. A mere trace of sulfate in the presence of phosphate, as I shall show presently, is sufficient to lead to the production of pigment. I have found that many samples of "C.P." phosphate obtained from reliable manufacturers contain a quantity of sulfate sufficient to vitiate the results, and I have consequently been compelled to prepare pure phosphates by recrystallization or by thorough washing.[14]

If the various species be grown in a solution of 0.2 per cent, asparagin, 0.1-0.5 per cent. sodium (or magnesium) chlorid, and 0.1 per cent. neutral sodium phosphate, the resulting turbidity is but little, if at all, greater than in the asparagin-phosphate solution alone. If, however, 0.1 per cent. of sulfate (sodium, magnesium, or potassium) be added to the asparagin-phosphate so-

lution, abundant multiplication takes place together with a rich development of the fluorescent pigment.

To determine the amount of sulfate necessary for the production of the pigment, solutions were prepared containing 0.2 per cent. asparagin; 0.1 per cent. neutral sodium phosphate; and respectively 0.1, 0.01, 0.001, 0.0001, and 0.00001 per cent. magnesium sulfate. All of the species except B. fl. putridus produced pigment in the presence of 0.01 per cent, and 0.001 per cent. sulfate nearly as well as when 0.1 per cent. was used; with the smaller amount of sulfate, the development of pigment was slower, but the final result almost as intense. With 0.0001 per cent. of sulfate a good development of color was brought about by all five species. In the presence of 0.00001 per cent. of sulfate B. viridans alone showed any well-defined development of pigment. There was the merest trace of color in B. fl. mesentericus, and the others were entirely without a tinge.

The nature of the base associated with the phosphorus and sulfur appears to be a matter of complete indifference. Sodium, potassium, and magnesium salts give similar results in whatever way they were combined. Even if ammonium phosphate and ammonium sulfate be used together, fluorescence appears, but it is somewhat less intense than in the presence of one of the bases mentioned above.

To determine the amount of phosphate necessary for the formation of pigment, solutions of 0.2 per cent. asparagin, 0.1 per cent. magnesium sulfate, and varying quantities of neutral sodium phosphate were inoculated in the usual manner. In the asparagin-sulfate solution containing 0.001 per cent. of the phosphate, good color was developed by all the species, being deepest in the cultures of B. viridans and B. fl. mesentericus. In the same solution containing 0.0001 per cent. of phosphate no pigment was developed by any of the species; the turbidity was, however, slightly more pronounced than

in the control tubes of simple asparagin-sulfate solution.

These organisms are able to produce the fluorescent pigment for a series of generations in such simple media as I have used. In a solution of 0.2 per cent. asparagin, 0.1 per cent. sodium phosphate, and 0.0001 per cent. magnesium sulfate, B. fl. albus is able to develop a fairly intense color. If from a culture in this medium a second tube of the same solution is infected, and the procedure repeated at intervals of three days, neither attenuation nor exaltation of the fluorescigenic power can be noticed after thirteen successive transfers. The same statement holds true of the action of B. fl. putridus in a solution containing 0.25 per cent. ammonium lactate, 0.1 per cent. sodium phosphate, and 0.1 per cent. magnesium sulfate.

The solutions of the ammonium salts of the organic acids, with the exception of the urate, contained respectively 0.5 per cent. of the ammonium salt and 0.1 per cent. each of neutral sodium phosphate and magnesium sulfate. Ammonium succinate, lactate, and citrate all proved to be substances well adapted for the production of the fluorescent pigment. The color appears more speedily in the succinate and lactate, and with most species becomes also more intense than in the citrate.

In the succinate solution all of the species but one developed pigment quickly and intensely. The color developed very tardily in the culture of B. fl. putridus, and never became intense. In ammonium lactate solution, a fine color developed within two days in the cultures of B. fl. albus, B. viridans, B. fl. tenuis, and B. fl. mesentericus; B. fl. liquefaciens was from ten to twelve hours behind the others at this stage, but eventually produced a very deep color; B. fl. putridus showed a much fainter tinge of color after ten days, and the color never became pronounced.

The ammonium citrate solution did not, on the whole,

lend itself to the production of pigment quite as readily as the lactate and succinate. B. fl. albus, B. fl. tenuis, and B. fl. mesentericus, indeed, seemed to flourish and produce pigment nearly as well as in lactate or succinate, but B. viridans and B. liquefaciens showed a decidedly less rapid growth, while B. fl. putridus caused only a very slight turbidity and developed no trace of color.

Ammonium tartrate solution afforded one of the most interesting examples of a difference between the cultures employed. B. fl. albus produced a rich coloration of the medium within the space of twenty-four hours. On the tenth day B. fl. tenuis likewise showed a slight tinge of color, and this slowly but steadily deepened, until, on the twenty-fifth day after inoculation, the color was as decided as in the tubes of B. fl. albus. None of the other species showed the slightest development of pigment, although a marked turbidity manifested itself in the tube inoculated with B. fl. liquefaciens, and a perceptible cloudiness appeared in the culture of B. fl. mesentericus and B. fl. putridus. The difference in the behavior of the several species in this solution was so striking that I repeated the experiment several times, always, however, with the same outcome. It is interesting to note in this connection that Thumm[15] states that the only species (among B. fl. albus, tenuis, erythrosporus, putridus, and viridans) that was able to produce fluorescent pigment in a tartrate solution (ammonium tartrate 0.5 per cent., potassium phosphate 0.05 per cent., magnesium sulfate 0.01 per cent., calcium chlorid 0.005 per cent.) was the one bearing the name of B. fl. albus. Thumm gives no description whatever of the various "species" that he used, but they were probably derived from the same source as my own cultures. Thumm's culture of "B. fl. tenuis" is recorded (p. 84) as showing "slight turbidity: no production of pigment" in the tartrate solution, while my culture designated by the same name is able to form a notable quantity of pigment, although

more tardily than B. fl. albus. In ammonium urate solution (urate 0.05 per cent., [16] sodium phosphate 0.1 per cent., magnesium sulfate 0.1 per cent.), B. fl. liquefaciens produces pigment more rapidly than the other species, but at the end of seven days B. fl. mesentericus and B. fl. tenuis rival it in intensity, and after eighteen days' growth B. fl. albus shows quite as deep a color as the species already named. There is at this time the merest dash of color in the tube of B. viridans, and none at all in that of B. fl. putridus.

Ammonium acetate solution gave on the first trial a slight turbidity with B. viridans, but no sign of growth with any of the other species. The acetate solution was found, however, to have quite a decided acid reaction, and on rendering it slightly alkaline with ammonia, all the species except B. fl. putridus became able to produce a very considerable quantity of pigment.

Ammonium oxalate solution is not adapted to the production of pigment although capable of supporting growth. B. fl. albus and B. fl. tenuis cause decided turbidity, but never develop any trace of fluorescent pigment even when alkali is added to the medium. The other species show varying degrees of cloudiness. If a more dilute solution be employed (0.05 per cent. oxalate), a faint tinge of color appears in the culture of B. fl. liquefaciens, and the merest suggestion of fluorescence is shown in the tubes of B. fl. albus, B. fl. tenuis and B. fl. mesentericus.

In ammonium formate solution the conditions for growth and pigment production are still less favorable than in oxalate; in the ordinary solution the tubes remain perfectly clear. If the solution be made slightly alkaline, however, a faint tinge of color appears in the culture of B. fl. liquefaciens, but the other species, while producing a slight turbidity, never form pigment.

INFLUENCE OF CONCENTRATION OF THE MEDIUM.

Considerable influence upon the production of pig-

ment is exerted by the degree of concentration of the medium. In Uschinsky's solution[17], which consists of glycerin 30-40 gm., sodium chlorid 5-7 gm., calcium chlorid 0.1 gm., magnesium sulfate 0.2-0.4 gm., dipotassium phosphate 2-2.5 gm., ammonium lactate 6-7 gm., sodium aspartate 3-4 gm., dissolved in 1000 c.c. of water, some of the species, notably B. fl. albus and B. fl. mesentericus, grow luxuriantly and produce a goodly quantity of pigment, but the intensity of color never reaches as high a point as in some of the simpler solutions, and the color assumes much earlier the yellow tinge which overtakes all old cultures. Some of the species, as for example B. fl. putridus, are unable to grow in Uschinsky's medium, and the tubes, although inoculated from a young active culture, remain perfectly clear. There is some lack of uniformity in regard to the behavior in this medium. B. viridans and B. fl. tenuis, for example, will sometimes multiply and produce considerable turbidity without forming pigment, and at others, under apparently identical conditions, will refuse to grow at all. The presence of glycerin is one of the unfavorable factors. If the medium be diluted 1:5 or 1:10, all of the species are able to grow and produce pigment.

A medium somewhat similar to Uschinsky's, but simpler, was compounded by Fränkel.[18] This consisted, in its final modification, of sodium chlorid 0.5 gm., ammonium lactate 6 gm., asparagin 4 gm., neutral sodium phosphate 2 gm., dissolved in 1000 c.c. of water. The solution was either amphoteric or slightly acid, and was made slightly alkaline "with a small quantity of caustic soda." In my early experiments all the species grew quite luxuriantly in this medium, but never produced any fluorescence, although the old cultures usually had a yellow tinge. The reason for this failure to produce pigment might at first be supposed to lie in the absence of sulfate, especially since color is developed when sul-

fate is added to Fränkel's medium. But that this is not the whole explanation is shown by the fact that, if the original medium was diluted 1:10, a very fair development of pigment took place. Investigation showed that some of the ingredients of the solution were not perfectly pure, but contained a trace of sulfate. The quantity of sulfate present, however, was not sufficient to permit of pigment production in the strong solution, although one-tenth of the same quantity was sufficient to permit of pigment production in a less concentrated medium. If Fränkel's medium be prepared with perfectly pure chemicals no pigment production occurs even when the solution is diluted.

The effect of concentration is well shown in experiments made with solutions of high phosphate content. In solutions of 0.2 per cent. asparagin, 0.0001 per cent. sodium sulfate, and, respectively, 1, 0.5, 0.2, 0.1 per cent. neutral sodium phosphate, B. fl. albus develops pigment most rapidly and intensely in the 0.1 per cent. phosphate solution. B. fl. putridus and B. fl. tenuis, on the other hand, develop pigment soonest in the 1 per cent. phosphate solution, and the former species does not develop any at all in the solutions with slighter phosphate content. As a rule, however, especially in solutions containing a larger amount of sulfate, a phosphate content as high as 1 per cent. interferes with the production of fluorescent pigment and the culture generally assumes a muddy yellow tint. The same thing occurs if a considerable quantity of ammonium salt be employed. B. fl. albus, for example, in a solution of 2 per cent. of ammonium tartrate and the usual quantities of phosphate and sulfate, imparts less of a fluorescent tinge and more of a yellow color to the medium, than with the ordinary 0.5 per cent. tartrate solution. This fact is of interest in connection with Lepierre's conclusions[19], which are based upon experiments made with 2 per cent. solutions of ammonium salts. The high acidity

of such strong solutions as he employed, however, was probably an even greater factor in the vitiation of his results than the simple concentration of the medium.

INFLUENCE OF LIGHT UPON PIGMENT PRODUCTION.

Pigment production is perceptibly affected by light. I have made no experiments with regard to the action of direct sunlight, but have confined myself to a comparison of cultures kept in the dark on a desk near the windows of a room into which no direct sunlight, but only north light entered; the former were kept in a locker in the same room and as nearly as possible at the same temperature, although variations of from three to four degrees were occasionally observed. These slight temperature variations were, however, sometimes on the one side, sometimes on the other, and I have seen no reason to infer that the course of pigment production is materially influenced by such slight fluctuations. It has invariably happened in these experiments that the cultures kept in diffuse daylight show a distinctly fainter color than the control tubes kept in the dark. In several instances fluorescence failed to appear in cultures grown in the light. This is true, for example, of a culture of B. fl. albus in a solution of 0.2 per cent. asparagin, 0.1 per cent. sodium phosphate, 0.0001 per cent. magnesium sulfate. In other solutions too, in which the amount of pigment produced is at best not great, a similar complete inhibition of the fluorescigenic power can be noticed. Thumm (l. c.) does not state whether the cultures in his experiments were kept in the dark or in the light, and it may be suggested that if the latter was the case some of his negative results (as, for example, that with B. fl. tenuis in ammonium tartrate solution) might be accounted for.

The question whether in such cases the light acts upon the pigment or upon the metabolic activity of the bacteria is a difficult one to come at. The turbidity of cultures kept in the dark and in the light seems to be

about the same. If cultures in which abundant pigment production has taken place be transferred to the light (this was done with a set of cultures in ammonium succinate solution), a very slight fading out can be noticed at the end of two weeks. The fading is accelerated by placing the tubes on the window-sill (north light), but even after the expiration of three weeks no very extensive divergence can be noted when the tubes are compared with the control tubes which have remained all the while in the dark. The cultures of some species, however, show a greater tendency to fade than others; the pigment produced by B. fl. albus fades out quite readily, while that formed by B. fl. tenuis retains its brightness with comparative persistence. The fading out consists in the gradual yellowing of the pigment, which continues until all trace of green is eliminated; cultures kept in the dark show the same change, but it takes place, as I have indicated, more slowly. The change is probably one of oxidation, and the acceleration of the process in the light is precisely what might be anticipated. The addition of an oxidizing agent, as dilute potassium permanganate, has a similar etiolating effect upon the pigment.

INFLUENCE OF THE REACTION OF THE MEDIUM.

The presence of acid checks the production of pigment. Even in slightly acid solutions where considerable multiplication may occur, pigment is not formed. The interference of the acid seems to be rather with the metabolic activities of the bacteria than with the pigment, as the following facts indicate. The pigment when it is once formed is not destroyed by acid, but simply rendered invisible. If a few drops of acid be added to a finely pigmented culture of any of the species employed, the color is completely discharged, but the addition of alkali brings it back as vividly as ever. On adding acid again and then alkali the same change again occurs, and this can be repeated for at least six times

upon the same culture without any perceptible weakening of the intensity of the pigment. When, furthermore, a well-developed culture is made quite strongly acid with HCl and allowed to stand for twenty-four hours, the color reappears when alkali is added with the same intensity as before. The existence of an aphanochromatic substance, at one time conspicuously visible in the form of the fluorescent pigment, at another colorless and not apparent, is clearly demonstrated by these experiments. This substance, however, is not formed in acid solutions.

The influence of acid upon the pigment is beautifully shown in the fermentation tube where the pigment acts as an indicator. In 3 per cent. glucose-broth (prepared from broth freed of muscle-sugar by the method suggested by Theobald Smith[20]), B. viridans for the first four to five days after inoculation develops no pigment although the broth becomes very turbid. No color appears when alkali is added to the broth at this stage, conclusively showing that the presence of acid interferes with the production of the pigment or its aphanochromatic double and does not simply mask the presence of this substance. After eight or nine days, however, pigment makes its appearance. In such a nutrient medium, then, there is a struggle between two of the vital activities of this organism, namely, its ability to produce acid and its power to form alkali. The latter "function" in this case ultimately gains the upper hand.

In 3 per cent. saccharose broth the course of events is exactly reversed. Saccharose is less easily fermented by this species and the result is that pigment is formed at the outset and a two days' growth is well colored. As the saccharose becomes converted into acid the color slowly fades out and at the end of four days it has vanished.

The pigment formed by all the species is at first, as has been shown by Thumm and others, a delicate robin's

egg blue, but as the solution becomes more alkaline owing to the bacterial growth, the color changes to green, and in strongly alkaline solutions is a deep green tint, showing no fluorescence. The addition of alkali to a solution containing the blue pigment produces at once the same change as is wrought more slowly by the alkali formed by the bacteria.

SUMMARY.

The upshot of my experiments may be summarized under the following heads:

1. The presence of both phosphorus and sulfur is essential to the formation of the fluorescent pigment.

The effect of almost infinitesimal quantities of sulfate in the presence of phosphate compels us to accept with some reserve the statements made by authors as to the production of fluorescence in media devoid of sulfur. Thumm's curious statement[21] that B. fl. albus, while it produces fluorescence in a medium composed of 1 per cent. ammonium succinate, 0.1 per cent. potassium phosphate, 0.04 per cent. magnesium sulfate, 0.02 per cent. calcium chlorid, and also produces a feeble green fluorescence when the magnesium sulfate is ommitted, produces no fluorescence at all if the calcium chlorid also be left out, is perhaps most easily explicable on the supposition that a small amount of sulfate was present as an impurity in the latter salt.

2. The nature of the base associated with the phosphorus and sulfur is not important.

Thumm observed, as I have done, that the omission of calcium chlorid alone from a nutrient solution containing potassium phosphate and magnesium sulfate exerts no perceptible effect on the production of pigment, but that the omission of the magnesium sulfate alone causes a marked diminution in pigment production; in my own experiments a total inhibition. From this he draws the singular conclusion that "so far as the formation of pigment is concerned, magnesium can not

be replaced by calcium." It is not necessary to point out the fallacy involved in such a deduction.

3. The conclusions that may be drawn regarding the dependence of the fluorescent "function" upon the molecular constitution of the ammonium salts may be best appreciated through an examination of the constitutional formulæ of the organic acids whose salts were employed. The list is arranged, as far as possible, in order of fluorescigenic value.

Asparagin,	$COOH.CH_2.CH.(NH_2).CONH_2$
Succinic acid,	$COOH.CH_2.CH_2.COOH$.
Lactic acid,	$CH_3.CHOH.COOH$.
Citric acid,	$COOH.C(OH).(CH_2COOH)_2$
Tartaric acid,	$COOH.CHOH.CHOH.COOH$.
Uric acid,	$NH.CO.NH.CO.C{=}C.NH.CO.NH$.
Acetic acid,	$CH_3.COOH$.
Oxalic acid,	$COOH.COOH$.
Formic acid.	$H.COOH$.

Lepierre[22], who studied the behavior of a species closely related to if not identical with B. fl. putridus, draws from his work the far-reaching conclusions that the fluorescence is intimately bound up with: first, the bibasicity of the acid; second, the existence in the molecule of at least two groups of CH_2. Conclusions analogous to these can not be deduced from my own work. The difference between acetic acid on the one hand and oxalic and formic acids on the other is certainly significant, but that neither the carboxyl (COOH) nor the methylene (CH_2) grouping is essential to pigment production is shown by the availability of urate. The difference between tartrate and succinate, as well as that between formate and acetate does, however, clearly indicate that, other things being equal, the presence of the methyl or methylene group is coincident with superior nutritive value and fluorescigenic power.

4. The presence of acid in the medium not merely conceals the existence of the substance to which the color is due, but interferes with those vital activities of the

bacilli, which, in an alkaline solution, lead to the production of that substance.

5. Diffuse daylight is unfavorable to pigment production.

6. If chemical substances that prove, when in certain proportions, favorable to growth and to the production of pigment be present in excess of a certain quantity, the production of pigment will be checked, although growth may be more abundant than before.

I may add, as an obiter dictum, that since the pigment is of no discoverable advantage to the organisms possessing the power of producing it, its production is probably purely incidental and not an essential vital act. The "fluorescigenic function," upon which some bacteriologists dwell, is in my opinion simply the expression of certain changes wrought by the organism upon the nutrient substratum in which it lives. When the substratum contains certain compounds, the metabolic activities of the organism adjust themselves to these conditions and the metabolic products differ correspondingly. It is purely a matter of accident and of no physiological significance that under certain conditions one of these metabolic products happens to be fluorescent.

Dec. 12, 1899.

LIST OF FLUORESCENT BACTERIA.

1. Bacillus aquatilis fluorescens (Lustig). Diagnostik der Bakterien des Wassers 64, 1893.

2. B. butyri fluorescens (Lafar). Arch. f. Hyg. 13:1, 1891.

3. B. chromo-aromaticus (Galtier). Compt. Rend. 106.

4. B. cyaneofluorescens (Zangemeister). Centralbl. f. Bakt. 18:34, 1895.

5. B. cyanogenus (Ehrenberg). Cf. Hueppe. Mitt. a. d. Kaiserl Ges. 2:—.

6. B. dentalis viridans (Miller). Die Mikroorganismen der Mundhöhle 316. [2d ed.]

7. B. erythrosporus (Eidam). Cf. Cohn and Miflet, Cohn's Beiträge 3:128.

8. B. fluorescens albus (Zimmerman). Die Bakterien unserer Trink- und Nutzwässer 18. Chemnitz. 1890.

9. B. fluorescens aureus (Zimmerman), op. cit. p. 14.

10. B. fluorescens capsulatus (Pottien). Zeitschr. f. Hyg. 22: 140. 1896.

11. B. fluorescens convexus (Wright). Memoirs National Acad Sciences 7:—. 1895.

12. B. fluorescens crassus (Flügge). Die Mikroorganismen 2:294. [3d ed.]

13. B. fluorescens foliaceus (Wright), loc. cit.
14. B. fluorescens immobilis (Flügge), loc. cit.
15. B. fluorescens incognitus (Wright), loc. cit,
16. B. fluorescens liquefaciens (Flügge). Die Mikroorganismen 289. [2d ed.]
17. B. fluorescens longus (Zimmermann), op. cit. p. 20.
18. B. fluorescens mesentericus (Tartaroff). Die Dorpater Wasserbakterien. 1891.
19. B. fluorescens minutissimus (Unna and Tommasoli). Monatsch. f. prakt. Dermatol. 9.
20. B. fluorescens mutabilis (Wright), loc. cit.
21. B. fluorescens nivalis (Schmolck). Centralbl. f. Bakt. 4 :545. 1888.
22. B. fluorescens non-liquefaciens (Flügge). Die Mikroorganismen 293. [3d ed.]
23. B. fluorescens ovalis (Ravenel). Memoirs National Acad. Sciences 8 :—. 1896.
24. B. fluorescens putridus (Flügge), Die Mikroorganismen 288. [2d ed.]
25. B. fluorescens putridus colloides (Tartaroff), loc. cit.
26. B. fluorescens Schuylkilliensis (Wright), loc. cit.
27. B. fluorescens tenuis (Zimmermann), op. cit. p. 16.
28. B. fluorescens (Lepierre). Ann. de l'Institut Pasteur 9 :643. 1895.
29. B. graveolens (Bordoni-Uffreduzzi). Fortschr. d. Med., 1886.
30. B. iris (Frick). Virchow's Archiv., 116 :292. 1889.
31. B. leucæmiæ canis (Lucet). Baumgarten's Jahrb. 1891 :319.
32. B. lupuliperda (Behrens) (cf. Lafar, Technical Mycology 166).
33. B. melochloros (Winkler and Schröter). Centralbl. f. Bakt. 9 :700. 1891.
34. B. oogenes fluorescens (5 varieties) (Zörkendörfer). Arch. f. Hyg. 16 :300. 1893.
35. B. proteus fluorescens (Jäger). Zeitschr. f. Hyg. 12 :525. 1892.
36. B. pyocaneus (Gessard). Thèse de Paris, 1882.
37. B. rugosus (Wright), loc. cit.
38. B. scissus (Frankland). Zeitschr. f. Hyg. 6 :398. 1889.
39. B. smaragdinus-fœtidus (Reimann). Inaug. Diss., 1887.
40. B. striatus viridis (Ravenel), loc. cit.
41. B. virescens (Frick), loc. cit.
42. B. viridescens non-liquefaciens (Ravenel), loc. cit.
43. B. viridis (Lesage). Arch de Physiol. 20 :212. 1888.
44. B. viridis pallescens (Frick), loc. cit.
45. B. viridans (Symmers). Brit. Med. Journ. 2 :1252. 1891.
46. B. viscosus (Frankland), op. cit. p. 391.
47. Bacterium osteophilum (Billet). Bull. Scient. de la France et de la Belgique. 1890.
48. Diplococcus fluorescens fœtidus (Klamann). Allg. Med. Centralzeitung. 1887 :1347.
49. Micrococcus fluorescens (Maggiora). Gior Soc. Ital. d'Igiene 16.
50. M. versicolor (Flügge). Die Mikroorganismen 177. [2d ed.]

BIBLIOGRAPHY.

1. I have also made some experiments with B. pyocyaneus, but owing to the complication due to the formation of at least two pigments by this bacillus, I am led to reserve my statements on this head for a subsequent communication.
2. O. E. R. Zimmermann, Die Bakterien unserer Trink- und Nutzwässer 18. Chemnitz, 1890.
3. Op. cit. p. 16.
4. Verhandl. d. naturhistor. Verein zu. Heidelberg. N. F. 5 : 536. 1897.
5. Flügge, Die Mikroorganismen, 2 : 293.

6. Die Dorpater Wasserbakterien. Inaug. Diss., 1891.
7. British Medical Journal 2:1252, 1891; cf. also Brit. Med. Jour. 1:113. 1893.
8. Op. cit. 2: 22.
9. Op. cit. 2: 30.
10. Flügge's Die Mikroorganismen, loc. cit.
11. Ann. de l'Inst. Past. 6: 801. 1892.
12. Ann de l'Inst. Past. 9: 643. 1895.
13. Beiträge zur Biologie der fluorescierenden Bakterien. Arb. d. Bakteriol. Inst. d. grossh. Hochschule zu Karlsruhe, 1895.
14. I am indebted to my friend Professor Stieglitz for many suggestions regarding the preparation and testing of pure salts.
15. Op. cit. p. 84.
16. On account of the comparatively slight solubility of the urate a smaller quantity was used than of the more soluble ammonium salts.
17. Centralbl. f. Bakt. 14: 316. 1893.
18. Hyg. Rundschau, 4: 700.
19. Ann. de l'Inst. Past. 9: 643. 1895.
20. Journ. Expt. Med. 2: 543. 1897.
21. Op. cit. 42-43.
22. Ann. de l'Inst. Pasteur. 6: 543.

THE ETIOLOGY OF SCARLATINA.

W. J. CLASS.

Numerous efforts have been made in recent years to discover the specific causative factor of scarlet fever. The most notable experiments along this line were those of Crajlcowski, Klein and Edington. Klein in a large number of cases isolated a streptococcus which he considered as the causative factor; this germ is also considered by a number of French observers to be the cause of scarlet fever. Klein, I believe, considered the throat as the gateway by which the infection entered. Crajlcowski in 1895 reported that he found in fifteen cases in which he examined the blood of scarlet fever patients a diplococcus present in comparatively small numbers. This diplococcus does not stain by Gram's method and, in general, stains feebly and quickly loses its color. Cultures were obtained in bouillon and upon solid media but not on gelatin. The development is said to be slow, and the colonies resemble small drops of dew, not more than one-third to one-half millimeter in diameter. It is pathogenic for mice, but not for rabbits. Crajlcowski does not claim that the etiologic relation of this diplo-

coccus to scarlet fever has been demonstrated. Edington isolated a number of micro-organisms from the scales of scarlet fever patients, among them a coccus which he named micrococcus capsaformis and a bacillus which he considered to be the causative factor of scarlatina. Numerous other germs, mostly bacilli, have been described as occurring in the scales of scarlet fever patients, but their relationship to the disease was never satisfactorily proven. In this connection a report by Behla published in the *Centralblatt fuer Bacteriologie* interested me particularly. Behla did not describe any germ, but he noticed that some pigs belonging to a peasant in whose family there were several typical cases of scarlatina, developed a scarlet rash. In order to see whether there was any connection between the scarlet fever in the peasant's family and the rash in the pigs Behla took some blood from one of the children having scarlet fever and inoculated a healthy pig with it, after a few days a scarlet rash appeared around the edges of the inoculation wound followed by desquamation. During the winter of 1897-98 the writer had occasion to examine a large number of cultures taken from the throats of persons suffering from various forms of angina. These cultures, numbering about 700 or 800, during the winter were grown on blood serum. On examining them I noticed that about every twentieth culture showed large diplococci mixed with the other germs present. During the early part of the winter I did not pay any particular attention to them, but toward spring I began to notice that they were most often present in cultures taken from patients having scarlet fever. During the following summer my time was occupied by other work and as there were comparatively few cultures to be examined I dropped the matter temporarily. Last autumn the germ again showed itself in the cultures and in an increasing percentage of the total number examined. I now began making cultures from the scales of scarlet

fever patients on blood serum, but without any very satisfactory results; the same germ which was noticed in the throat cultures again appeared but I could not isolate it and it did not appear to be constantly present. I have subsequently discovered that it was constantly present, but on account of its polymorphous character it appeared to be a different organism. As I had been working for the last two years with a culture medium composed of gycerin agar agar to which about 5 ounces of sterilized garden soil had been added the thought occurred to me that perhaps the results would be better with this medium. And from the results of my experiments in cultivating scales, throat secretions and blood from scarlet fever patients on this medium I arrived at the conclusion that the germ which I am about to describe is probably the specific causative factor of the disease.

Morphology.—A diplococcus, polymorphous in character but resembling as ordinarily seen in slides made from fresh cultures grown on my medium, a very large gonococcus. This biscuit-shaped appearance is best seen in specimens that have been but lightly stained. Tetrads are frequently seen and probably they denote the beginning division of the organism as I shall attempt to show to you in some specimens to-night. In very old cultures grown under favorable conditions it shows as an enormous coccus having a slight cupped appearance, the dividing line between the two portions of which it is composed being very indistinct in the more deeply stained specimens, a crescentic appearance of the germ is also sometimes seen under these conditions. By the division of the large diplococcus a number of smaller organisms are formed which group together and do not appear as diplococci during the very early stages of their growth. In young cultures grown from the blood of a scarlet fever patient the germ is usually seen as a diplococcus, both segments of which are globular. Strepto-

coccus forms are occasionally, though rarely met with, as are also single cocci. Usually, unless in spreading the culture on the slide it is rubbed very hard, these cocci occur in bunches of from 10 to 50 which bunching is due to the large amount of glutinous intercellular substance by which they are united. The organism has no capsule although at one period of its growth it has the appearance of having one, does not show any pores, has no flagellæ and examined by the hanging drop method, does not show any independent motion.

Staining.—Specimens derived from pure cultures were stained with a number of the anilin stains. With a watery solution of methyen blue very pretty pictures were obtained, especially when only lightly stained; carbol-fuchsin also stains it well and brings out its characteristics. It also stains with Bismarck brown and with Pitfield's flagellæ stain. Fresh cultures do not stain very deeply, however, with any of the stains mentioned. It is decolorized by Gram's method though not to the same extent as the gonococcus, the larger variety of the germ holding the stain better than the smaller.

Biological Characters.—The culture medium on which this germ grows by preference is prepared as follows: Glycerin agar agar is made according to the method generally used. To this is added about 5 per cent. by weight of black garden earth which has been rendered sterile by discontinuous heating. The garden earth is first dried thoroughly, then sifted through a very fine hair sieve until it is reduced to a fine powder, all particles of gravel, sand, etc., being removed. It is then mixed with sufficient bouillon to form a thin paste. This is boiled for an hour, enough sterile bouillon being added from time to time to replace that evaporated by boiling, it is then set in a warm place for a few days to allow the spores found in the earth to develop; it is then again boiled for an hour after which it is again set aside for a few days. This procedure is repeated until

no growth can be developed. It is then added to the agar agar, which mixture is also boiled for about 30 minutes, and then put aside for a few days to see if any germs develop. Should this be the case, the mixture is again boiled and tested as before. On this medium the scales from a scarlet fever patient are placed with a sterile platinum loop, and the tubes put in an incubator, the temperature of which is kept at about 35 C. In from forty-eight hours to one week small whitish-gray semi-transparent colonies will appear along the track of inoculation and around the scale. These colonies are isolated at first, but subsequently coalesce. Their diameter varies somewhat, but in general is about 1 mm. On taking up some of the material of which the colony is composed with a platinum needle, it is seen to be glutinous, being drawn out in threads like glue. If the culture medium is dry or when the colonies are old they lose their viscidity and become darker in color. On the blood-serum furnished by the Health Department for the diagnosis of diphtheria there is a growth, but it is more meager than on the medium described by me, the earth agar agar being especially adapted for growing the germ from the scales and throat secretions, for blood cultures the serum will do almost as well, as the germ is not mixed with other organisms. On glycerin agar agar it grows feebly and does not show its characteristic features, which caused me to believe for a time, that the growth on this medium was due to a contamination. On gelatin I have not been able to get any growth. In bouillon they do not appear to multiply. Milk is not affected by these organisms, although they apparently multiply in it.

The germ described has been cultivated from the scales of 74 cases of typical scarlatina, from the throats of about 50 cases of angina accompanying scarlatina and from the blood of 16 cases of scarlatina.

CONTROL EXPERIMENTS.

1. In order to ascertain whether the germ was present in the throats of persons who had not to their knowledge been exposed to scarlet fever I examined 36 cultures from as many different persons; the diplococcus scarlatinæ was found in 8 specimens but only in very small numbers while in the angina of scarlet fever it was invariably present in great numbers.

2. The thought occurred to me that the germ might be a normal inhabitant of the human skin; to eliminate this point I examined scales from 23 persons not afflicted with the disease, the scales being mostly those of dandruff, with the result of finding it present in 3 instances.

3. Examination of the blood of 10 persons in a healthy condition, the blood being taken with the same precautions as those observed in collecting it from the scarlet fever patients, gave an absolutely negative result as far as any growth was concerned, while in the cases of scarlet fever the germ could almost invariably be cultivated during some period of the disease between its onset and the full development of the rash.

PATHOGENESIS.

Rabbits and guinea pigs in good condition were inoculated by subcutaneous injection of a pure culture, by scarification and inoculation of the wounds produced and by injection into the abdominal cavity, without producing the slightest results. The negative results of the subcutaneous injections show that the germ is no pus producer, at least not in the species mentioned. Subsequently two guinea-pigs whose vitality had been lowered by keeping them for a period of about a month in a dark place were infected with approximately the same amount of a pure culture as was used in the other animals. On the third day after the inoculation the animals began to show signs of illness, the rectal temperature being increased by about 2 de-

grees F. One of the animals died on the eighth, the other on the tenth day after inoculation. Post-mortem examination showed a pronounced nephritis in both animals. The cortex of the kidney after removing the capsule showed numerous minute hemorrhages, on cutting through the kidney the substance seemed softer and more friable than is normally the case. The pyramids stood out plainly and were of a dark red color, the entire organ appearing congested and edematous. Culture tubes were inoculated from the kidneys and a pure growth of the organism described by me was obtained. The other organs of the animals showed no macroscopical changes.

As Behla had shown that swine were apparently susceptible, a number of these animals were inoculated with cultures derived from the scales of a virulent case of scarlatina.

Animal No. 1.—Weighing about 20 lbs., in good condition, skin perfectly normal, no sign of any skin lesion. Rectal temperature 101½ F. About 1 c.c. of a culture of the diplococcus was mixed with about 3 c.c. of distilled water and injected into one of the veins of the ear. During the first four days the animal showed no signs of any disturbance. On the fifth day the animal became restless and the rectal temperature rose to 103 F. On the seventh day a pronounced reddening of the skin was noticed; most marked on the abdomen; this lasted about 36 hours. On the tenth day, the animal began to scale, the scales being most numerous on its abdomen and ears. Cultures made from the blood and scales showed the same organism as was injected. This animal was killed and on examining its organs the kidneys were found to present a similar condition as was noticed in the kidneys of the guinea-pigs, with the excepting that the right kidney showed a small abscess in the cortex. Cultures taken from the kidneys again showed the same germ.

Animals No. 2, 3 and 4.—Weighing 12, 16 and 19 lbs. respectively, were inoculated in a similar manner with similar results in regard to the rash and scaling, the same germ being found in their blood and scales. In the third animal injected the eruption was more of a papular character and the reddening was not so marked.

Animal No. 5.—Weighing about 25 lbs., was injected subcutaneously in the abdominal region about 12 days ago, the culture used being the fifth generation of the one used in the previous experiments, no reaction except a rise in temperature of about 2 degrees on the fourth day after the injection was noticed up to the present time. I wish to state that the cultures used in these experiments were not isolated by means of "platten gressen," but I am quite certain that they were not contaminated by other germs, as repeated careful examinations showed and as the cultures from the blood and kidneys of the animals did not show any admixture. The reason why I did not isolate the germs by means of the process mentioned was on account of the fact that their vitality is destroyed by heating, the cultures obtained by isolating the germ by means of the plate method growing very poorly.

Before concluding, I would like to mention briefly a few differential points between this germ and similar ones that have been found in the skin and nasopharynx.

Micrococcus tetragenous subflarus.—Flat, dirty white colonies with shining surface, turns brown at the margins after three or four days.

Micrococcus tetragenus versatilis.—Colonies, pale yellow, which later become orange colored. Grows profusely on ordinary culture media; takes Gram's stain. Is almost universally present.

Diplococcus coryzæ.—Grows readily upon gelatin plates, forms white glass-like slightly elevated colonies.

Diplococcus albicans tardus.—Much smaller, grows much slower, dark yellow growth on gelatin. This germ is found on the surface of the body and in the air.

Micrococcus cumulatus tenuis.—Found in nasal mucus, large cocci associated in masses. Colonies are oval and perfectly transparent.

Micrococcus albus liquifaciens.—Liquefies gelatin readily, perfectly white shining layer on agar agar.

Diplococcus fluorescens fetidus.—Found in posterior nares, quick growth, brownish gray layer, liquefies gelatin readily.

Micrococcus of Demme.—Found in pustules of pemphigus acutus. Growth on agar agar has stalactite-like outgrowths and club-like projections. Colonies milk-white in color, never transparent.

May 8, 1899.

KLEIN'S "BACILLUS ENTERITIDIS SPOROGENES."

ADOLPH GEHRMANN.

In 1895 Klein[1] described the results of his bacteriologic findings in certain cases of acute diarrhea occurring in St. Bartholomew's Hospital in London. From the discharges of these cases he isolated and studied an anaërobic spore-bearing bacillus, and concluded that it was the cause of the sickness. Further, the same bacillus was isolated from the milk supplied to patients and the relation between the milk and the sickness was established because all those who became sick had partaken of this milk. Cultures were toxic for guinea-pigs. Klein offered the name Bacillus Enteritidis Sporogenes for the species.

In regard to the distribution and biology of this species of bacterium Klein has made further report. He[2] demonstrated its presence in 9 out of 13 samples of milk, 3 of them being sterilized, and 10 ordinary market milk. He has shown[3] the spores of the bacillus to be present in cases of summer diarrhea in children and of cholera morbus in adults. In 11 post-mortems upon children dying with summer diarrhea, the bacillus was found in 4. Klein[4] has reported finding the bacillus outside of the body in the following places: in the sewage of London and other English cities, and in the drains from St. Bartholomew's hospital; in samples of sewage from a number of stations for the treatment of sewage; in water of a number of streams in England, scrapings from Pasteur filters being examined; in horse-manure and garden earth; in the dust and dirt of streets.

Wild[5] found the same bacillus in street sweepings, but not in cow-dung.

From these reports it is clear that Klein's bacillus is widely distributed and occurs especially in the presence of active decomposition. No observations as yet show that its normal habitat is the intestine. Its abundance in horse manure may be accounted for by its probable presence in the dirt eaten with the hay, while the absence in cow dung may be due to failure to reach the spore stage at the time of discharge.

CHARACTERS OF KLEIN'S BACILLUS.

Isolation.—Cultures are made from the suspected material in glucose gelatin, heated to 80° C. for 10 or 15 minutes, and grown under anerobic conditions in test tube or plate culture show, in the course of 48 hours, liquefaction in the lower portion of the gelatin. Microscopical examination shows bacilli with rounded ends, some in short chains, two or three, but never in long chains. In hanging drop there is slight motility. These bacilli stain by Gram's method. Milk is also an excellent medium and shows characteristic coagulation. From

such cultures subcutaneous injections are made and if the animal dies pure cultures are obtained by anerobic plate cultures.

CHARACTER OF GROWTH.

Glucose gelatin inoculated in the deeper portion shows liquefaction in 24 to 48 hours to just below the surface. When the gelatin is inoculated in the usual way, making a stab, gas formation is observed in 24 hours, and there is very slight liquefaction of the gelatin, 8 to 20 days being required for complete liquefaction to take place.

The rapid liquefaction or the formation of gas with slow liquefaction indicates spore formation on the one hand, or its absence in the culture on the other.

Milk inoculations show no change during the first 24 hours, after which there is slow coagulation of casein and its separation into an upper and a lower layer, with clear fluid between. Gas is actively produced but spores do not form in the milk culture. When young gelatin cultures are transferred to milk these changes take place more rapidly and may even be complete within 24 hours. Anerobic cultivation on agar shows brownish round colonies. The potato shows very slight growth, smeary in character and not characteristic. Blood serum is liquefied.

ANIMAL EXPERIMENTS.

When .5 to 1 c.c. of a few days' old gelatin or milk culture is inoculated subcutaneously in an average-weight guinea-pig symptoms of depression are noticed in from 6 to 8 hours, and the animal dies in about 24 hours. Smaller doses cause temporary depression with local edema. The post-mortem examination shows extensive subcutaneous edema and emphysema. The superficial layers of skin with the hair rub off easily; and there is often a complete separation of the subcutaneous tissues from the underlying muscles. The most disagreeable odor is present. Bloody fluid is sometimes found

in the peritoneal cavity or in the pleura, and there is slight enlargement of the spleen. Other internal organs are not materially altered.

Microscopical examination shows the bacillus to be present in large numbers in the subcutaneous exudate, singly and in twos or threes, but never in long chains. Very few bacteria can be found in the internal organs or in the blood. Reinoculations of animals from the subcutaneous fluid show it to be extremely virulent. Older cultures containing mostly spores are not virulent, but by their active cultivations to the second and third generation, they may again become pathogenic.

DIFFERENTIATION.

This bacillus is closely related to the bacillus of malignant edema and to the bacillus butyricus of Bodkin, but there were differences in the culture and in the pathogenic properties that were sufficient for Klein to consider his bacterium as a new species.

Pure cultures of malignant edema bacillus give in inoculation experiments a clear bloody fluid with very slight or no formation of gas. The bacillus is found in great numbers in this fluid and long threads of bacilli are especially noticeable.

The experiments of Fluegge, Fraenkel and Simonds have noted the active formation of the gas in animals inoculated with garden earth for purposes of isolating the malignant edema bacillus, and it has been considered by them that this gas formation was due to the presence of the associated bacteria.

The chief differentiating points as proposed by Klein for his bacillus from that of malignant edema are the following: Bacillus enteritidis sporogenes stains by Gram's method. It does not form long threads either in cultures or in inoculated animals. Gelatin is more readily liquefied. Milk is coagulated in two layers in a characteristic manner, and no spores are formed in the milk cultures. From the bacillus butyricus of Bodkin

it is differentiated by the fact that the Bodkin bacillus is not pathogenic.

Special interest has been aroused in regard to Klein's bacillus by the recent report of Clows to the London County Council. In this report, which is preliminary, it is stated that the spores of bacillus enteritidis sporogenes were found in abundance in sewage examinations that were made in connection with the investigations of the Londan sewage, and it is further suggested that its presence may become one of the most delicate and valuable evidences of sewage pollution of potable water. With the possibilities in view it seems interesting to determine the presence of this bacterium in sewage and also to study its relation to polluted drinking water. My observations have, so far, been confined to Chicago river water and sewage taken directly from sewers, and upon the samples collected from the city water supply in making the daily analyses for the department of health.

The method of procedure was to plant from .5 to 2 c.c. of sewage or water to tubes of recently sterilized milk; to heat these for 10 minutes at 80° C.; and to keep the cultures after Buchner's method, in the incubator. If the characteristic coagulation of the milk appeared. 1 to 2 c.c. of the clear fluid in the culture tubes was injected into guinea-pigs. If death occurred further cultures were made at post-mortem. To obtain pure cultures plate cultures have to be made and cultivated under anerobic conditions in hydrogen.

Forty-two specimens of sewage were examined. Experiments were conducted on the regular samples of city water received for daily analyses, cultivations being made on 130 samples during March, April and May, 1899. Incidentally 16 samples of milk, 8 of garden earth and 1 of cheese, were also examined.

EXAMINATION OF SEWER WATER.

Of the forty-two samples examined thirty-one were

from the Chicago River at La Salle street, taken 18 inches below the surface. Nine were from the sewer outlet at Washington street and the river, and two from the 35th street sewer at its outfall into the lake.

All milk cultures to which the river water had been added and then heated to 80° C. coagulated within 24 hours, after being placed in the incubator. Gas formation was marked and the casein was firmly coagulated into irregular masses. The fat of the cream was set free and floated as oil drops. Animals were not inoculated from all of the milk cultures but eight cultures that were tested for pathogenic properties promptly killed the guinea-pigs in 20 to 36 hours. In each case the typical local gangrene with empyema as described by Klein was present.

It goes without saying that further examination of the gangrenous areas showed several varieties of bacteria present. By diluting drops of the fluid in the gangrenous tissues and making agar plates colonies were obtained under anerobic cultivation in hydrogen. From these pure cultures were obtained. A comparison of these cultures to those described by Klein warrants the assertion that the same species of bacterium caused the death of the animals.

The examination of animals that have died from the typical gangrene have resulted as follows:

The tissues about the point of inoculation feel soft and the hair rubs off easily. Fœtid odor. Opening into the subcutaneous tissues it is seen distended with gas, lifting it from the deeper muscles. Some grayish serous fluid is in these spaces.

Slides made direct from the tissues show numerous bacilli, short with round ends and in chains of seldom over 4 or 5. Cocci are sometimes seen.

Anerobic cultures in hydrogen on agar plates have shown in most instances three colonies; irregular, gran-

ular gray colonies; thin, flat, brownish, smooth colonies; and very thick, wrinkled colonies.

Microscopically these are all shown to contain spore-forming bacilli, appearing much alike—those of the last described colonies are actively motile, the others but slightly. When the bacteria from these colonies are inoculated into milk, the first two cause coagulation and gas formation; the third shows coagulation with precipitation of most of the casein and very slight gas production. Injection of animals shows only the cultures from the second, or brownish colonies to be pathogenic. The third colony gives cultures growing in oxygen, and has characters of growth much like the potato bacillus. I found that the gas production remains as a prominent feature of these cultures only when very actively cultivated.

All of the milk cultures from sewer water coagulated, but of seven guinea-pigs inoculated only five died of gangrene. One of the samples from the 35th street sewer did not cause coagulation of milk when the culture was made 2 hours after the collection of the sample, while three days later the same water caused typical coagulation when again inoculated. From these experiments it appears certain that bacteria of the species described by Klein or very similar to these are practically always present in the sewage of this city.

I am not ready to admit that all of the animals inoculated were killed by the bacillus enteritidis sporogenes, but it is at least clear that the group of bacteria to which this species belongs was present.

EXAMINATION OF CITY WATER.

From the experiments made on these samples it would not appear that search for Kelin's bacillus is of great value in determining sewage pollution, at least not for the Chicago water supply. This is because our results have practically all been negative. This has been true even during a recent period of pollution when the bacil-

lus coli communis was abundantly demonstrated. Klein suggests the use of the Pasteur filters as an aid to isolating the spores from water. This might appear satisfactory as an experiment, but in practical water examination I have found that the extra work and care involved in arranging for filtration in this manner is not repaid in the results. Further, it does not appear that the Bacillus Enteritidis Sporogenes is a normal intestinal inhabitant, and can not therefore be compared with Bacillus Coli Communis in significance when found in water.

Of the large number of city water samples cultivated anerobically in milk after being heated to 80° C. only in two instances were pathogenic results obtained with the cultures. Many of the milk cultures became coagulated but usually without gas formation or firm coaguation of the casein indicative of Klein's bacillus. Anerobic plate cultures of water heated to 80° C. gave but few colonies. The bacillus butyricus was identified among them. During this period the regular examination showed 20 to 25 per cent. of samples containing *bacillus coli communis.*

I am inclined to look upon this failure as being due to the attenuation of the bacterium similar to that which occurs in cultures when they are preserved for some time. This has been noted by Wild, some cultures being so atypical as to be scarcely pathogenic at all.

In the examination of a few samples of city milk, the specimens being taken from wagons in the course of regular inspection, no pathogenic effects were obtained with cultures prepared in the manner described. I can not agree as yet that this group of bacteria is abundantly present in milk, at least not in the spore stage when the milk is fresh.

The greatest difficulty that appears during a study of these pathogenic anerobic bacteria is due to the readiness with which they lose their pathogenic properties. Hib-

ler[6], in a very recent report of a study of 15 varieties of anerobic bacilli makes special note of this fact. I have considered our failure to find pathogenic anerobic bacteria in the city water samples as being due to this attenuation.

Another factor of great importance is the association of species in the material used for experiments in the first steps of isolation. It is not to be expected that the results of experiments with mixed cultures will be the same as when pure cultures are used. The results of animal inoculation are so quickly fatal when young mixed cultures are used that the association of species must have much to do with the virulence noted. Hibler divides these bacteria into three groups, based upon pathologic anatomical findings at the post-mortem of inoculated animals.

The first group represented by tetanus—in which there is practically no spread of the bacteria from the point of inoculation.

The second group represented by malignant edema, in which there is marked bloody edema, slight gas formation, but little spread into internal organs.

The third group, represented by the bacillus enteritidis sporogenes, in which there is abundant gas production and stinking decomposition, also with little extension of bacteria into the internal organs.

For the reason then that the characters of Klein's bacillus and also the group to which it belongs do not remain permanently characteristic, but change rapidly as the cultures are preserved for a longer period, it would not appear that this species offers a ready indication of sewage pollution.

June 12, 1899.

BIBLIOGRAPHY.

1. Centralbl. f. Bakter., 1895, xviii, 737.
2. Ibid., 1897, xxii, 113.
3. Ibid., 1897, xxii, 577.
4. Ibid., 1898, xxiii, 542.
5. Ibid., 1898, xxiii, 913.
6. Ibid., 1899, xxv, 513, 593, 631.

THE INFLUENCE OF ALKALIES AND ACIDS IN EMBRYONIC DEVELOPMENT AND GROWTH.

J. LOEB.

It was His, who first pointed out that the differentiation of the body form is brought about by dissimilarity of growth of the various elements. We know that certain conditions will modify the growth. Increase of temperature (within certain limits) for instance, will hasten the growth, while a lowering will retard it. This, however, is not the cause for the dissimilarity of growth in embryonic development. I have pointed out another condition, namely, the taking up of water. "Tubularien" will grow faster when the amount of water is increased and their growth is retarded when the amount is decreased. The water acts first mechanically as well as chemically. If we wish to hasten the growth we must seek to promote the synthetical processes, especially the increase of oxidation. We know that weak alkalies have the effect to increase oxidation. Our blood is slightly alkaline, if we diminish the alkalinity of the blood, by neutralizing with an acid, the process of oxidation becomes then lessened. For that reason I expected that the introduction of alkalies would hasten the embryonic development while acids would retard the development under any circumstances.

Experiments with the eggs of sea urchins (Arbacia). —The eggs of sea urchins were impregnated in normal sea water and afterward placed in various acid and alkaline solutions, usually 5 to 10 minutes after impregnation. The alkaline solution consisted of 100 c.c. sea water to which is added various quantities of 1-10 per cent. of normal NaHO solution. All the alkali does not remain in solution, but part falls to the bottom in combination with magnesium and calcium as magnesium

—and calcium hydrate. The precipitate should be removed by filtration as it hinders the development of the eggs. By the addition of 2 c.c. of 1-10 normal alkaline solution there is formed only a slight precipitate, which is harmless and filtration can usually be dispensed with.

The acid solution consists of 1-10 normal HCl solution. This acid causes no precipitation in sea water.

In comparing the furrowing of the arbacia eggs in alkaline solution (1½ to 2 c.c. of 1-10 normal NaHO to 100 c.c. of sea water) with those in normal sea water, it will be found that the furrowing in those of the alkaline solution has been hastened. This is more evident at the 64th cell stage. Furthermore, it was found that the movement of the blastulæ begins earlier when in the alkaline solution than in the normal sea water. The eggs were impregnated in one case at 9:30 and at 3:15 the embryos swam lively around in the alkaline solution, while those in the normal sea water were still motionless. In another case the impregnation took place at 10:45 and at 4:20 lively movement was seen in the blastulæ. In a third experiment the impregnation occurred at 11:00 and at 4:20 all the larvæ swam back and forth in the alkaline solution (1.5 c.c. 1-10 normal NaHO to 100 c.c. of sea water) while those in the normal sea water were still motionless. Later observation showed that movement in the latter began first at 4:40. Quite a difference in time.

When the examination was continued the following morning it was found that the eggs in the alkaline solution were in the pluteus stage, while those in the normal sea water were only in the gastrula stage. Not only is there a difference in the development, but also a difference in size. When examined after 48 hours, both those in the normal and alkaline solutions are in the pluteus stage, but those in the alkaline solution are larger and their arms are longer.

The solution acts best when 1½ to 2 c.c. 1-10 normal

NaHO is added to 100 c.c. of sea water. The addition of larger quantities as 3, 4, 5 and 6 c.c. 1-10 normal NaHO has no favorable influence, while less than 1 c.c. 1-10 normal NaHO is without effect.

Experiments with acid sol. show that the development is either retarded or checked. It was found that the eggs which were placed in vessels containing 1 c.c. 1-10 normal HCl to 100 c.c. of sea water began furrowing at 11:50, while those of the same culture in normal sea water began at 11:35. In vessels containing 2 c.c. 1-10 normal HCl, furrowing first began at 12:20, while the eggs in the normal sea water were at the 8th cell stage.

In 3 c.c. 1-10 HCl no furrowing took place.

The eggs in solutions of 1 to 2 c.c. 1-10 HCl developed into normal blastulæ, but the development takes place considerably slower than in those of the normal sea water. The eggs in the normal sea water were just as much ahead of those in the acid sol. (100 c.c. sea water + 1 c.c. 1-10 HCl sol.) in their development as the alkaline eggs were ahead of those in the normal sea water.

The addition of ½ c.c. 1-10 normal HCl sol. to 100 c.c. sea water has no marked influence in the development of the embryos.

Experiments with fish embryos (Fundulus).—In earlier works I have shown that fundulus are extraordinarily insensible to the concentration of the surrounding sea water, therefore I was greatly surprised to find the eggs of fundulus very susceptible to acids like HCl. The addition of 2 c.c. and 3 c.c. of a 1-10 normal HCl sol. to 100 c.c. of sea water retarded considerably their development and lengthened the period stage of (slipping out) eruption. The addition of 4 c.c. of 1-10 normal HCl to 100 c.c. of sea water usually kills most of the eggs in the first 24 hours, and only a few are capable to furrow in this solution. Addition of alkalies

to sea water has hardly any influence on the furrowing and development of the eggs.

It was found, however, that the addition of various quantities of alkalies to *fresh water* gave marked results. For instance, the addition of 6 c.c. of a 1-10 normal NaHO sol. to 100 c.c. *fresh* water showed that the embryos slip out so much quicker than those in normal fresh water. The addition of more than 6 c.c. retarded the development, while in 12 c.c. of a 1-10 normal NaHO sol. to 100 c.c. fresh water, it was found that only a few are capable to develop and slip out, the rest undergo destruction. With addition of 15 c.c. 1-10 HCl, development of the eggs may occur, but no eruption was seen.

The fundulus embryos are remarkably susceptible to acids when added to *fresh water*. The addition of 2 c.c. 1-10 normal HCl sol. to 100 c.c. of fresh water, kills all the eggs in a short time (with the addition of 3 c.c. HCl 1-10, etc., development still took place). Even 1 c.c. 1-10 HCl, etc., kills usually most of the eggs.

The results from the foregoing experiments show the fact that weak alkalies hasten the development and growth of arbacia-larvæ. The amount is surprisingly small—1½ to 2 c.c. 1-10 normal NaHO sol. (6-1000 per cent. of NaHO) acids have only a retarding influence on the development and growth. The cause for this action of weak alkalies and acids in the development and growth is to be found in the fact that weak alkalies in the living substance promote oxidation, while acids lessen the process of oxidation and in that way hinder the synthetical processes.

November 14, 1898.

Bertha Van Hoosen presented specimens of monstrosities in the fœtus. October 11, 1897.

D. W. Graham presented specimens of an excised carbuncle. He also exhibited some X-ray pictures, and showed how they may give entirely false ideas regarding fractured bones. November 8, 1897.

H. M. King exhibited specimens of stained blood from a case of pernicious anæmia. November 8, 1897.

E. R. Le Count made a microscopic exhibition of sections of lung and placenta which had been hardened in Müller's fluid and other chromic compounds. They showed a homogeneous material precipitated from the blood which reacts like colloid with Van Giesen's stain. November 8, 1897.

F. C. Schaeffer exhibited several examples of urinary vesical, and biliary calculi, removed during operation, January 10, 1898.

H. Froelich read a paper upon "The Etiology of Rheumatism and its Treatment, Including Serum-Therapy. January 10, 1898.

Eliza H. Root reported a case of epileptiform seizures in a child apparently due to nasal obstruction. March 14, 1898.

A. J. Ochsner demonstrated specimens of lipomata; 1, a large annular lipoma of the neck; 2, a diffuse lipoma of the knee following trauma; 3, a fibro-lipoma from the region of the parotid gland; 4, a large subaxillary lipoma. April 11, 1898.

M. Herzog exhibited microscopic specimens of a sarcoma, showing phagocytic cells. October 10, 1898.

J. Holinger demonstrated specimens; 1, foreign body (tampon) in the antrum of Highmore; 2, epidermoidal disk from the external auditory meatus; 3, necrotic malleus; 4, nasal polypus. November 14, 1898.

Emil Ries. "Syncytioma and its Possible Relation to Acute Yellow Atrophy of the Liver." December 12, 1898.

E. O. Jordan spoke upon the bacillus pyocyaneus and its pigments. June 12, 1899.

E. R. Le Count demonstrated microscopic specimens showing foreign body (cholesterin) giant-cells. June 12, 1899.

INDEX OF SUBJECTS AND NAMES.

Acromegaly, report of a necropsy in a case of..... 89
Amebæ, improved method of staining..... 235
Amnion, lymph-stomata in..... 342
Anemia, splenic..... 364
Aneurism of abdominal aorta..... 173
of coronary artery..... 174
of right ventricular wall..... 168
Aorta, abdominal, aneurism of..... 173
senile arteriosclerosis..... 174
Arteriosclerosis, syphilitic..... 176
senile, in aorta..... 174
Atheromatous abscesses in the aorta..... 174
Bacillus enteritidis sporogenes..... 533
hydrophilus fuscus..... 462
pyocyaneus, infection by..... 497
pyocyaneus and its pigments..... 547
Beffel, John Marshall..... 86, 311
Blood, from pernicious anemia..... 546
Brain, cysticercus cellulosæ of..... 14
neuroglioma ganglionare of..... 49
psammo-scarcoma of..... 49
tubercle of..... 49
tumors of..... 49
tumor of, showing a peculiar form of degeneration... 67
Brennecke, Herman A..... 211, 446
Bronchitis, exudative..... 143
fibrinous, a case of..... 136
Brown, W. I..... 178
Bullen, F. W..... 126
Calculi, vesical and biliary..... 546
Capps, J. A..... 174
Carbuncle, excised..... 546
Carcinoma, diffuse, infiltrating of stomach..... 205
of stomach with retrogressive lymphatic transport... 198
of ileum..... 198
of gall-bladder associated with gall-stones..... 175
of liver, secondary to tumor in gall-bladder..... 175
of pharynx with extensive and erratic cornification... 195
Cecum, chronic hyperplastic tuberculosis of..... 241
Cerebrum, glioma of..... 42
Chapman, George L..... 121
Cholesterin, giant-cells..... 547

Chordæ tendinæ, aberrant 145
Circulatory system 145
Class, W. J. 525
Coates, W. E. 173, 419
Colloid-like material precipitated from blood by chromic compounds 546
Congenital occlusion in duodenum, etc 185
Cook, Edgar P., Jr. 130
Cornification, erratic, in carcinoma 195
Coronary artery, aneurism of 174
Corpus luteum cyst, calcareous degeneration of 302
Cotton, A. C. 168
Councilman, W. T. 68
Crowder, T. R. 156, 241, 276
Cysticercus cellulosæ of brain and spinal cord 14

Dermatitis, blastomycetic, a case of 411
blastomycetic 419
Diamond, I. B. 14, 235
Digestive system 175
Diphtheria, antitoxin in 446
Ductless glands 89
Duodenum, congenital occlusion, etc 185
Dysentery, amebic, a case of 235
amebic, complicating noma in an adult 180

Ear, specimens of 546
Eisendrath, D. N. 67, 174, 276, 283, 497
Embolism, pulmonary, causing sudden death 134
Embryonic deevlopment and growth, influence of alkalies and acids in 542
Endocarditis 172
Epileptiform seizures in a child, etc 546
Eye, the 68
acute keratitis in the rabbit 68
glioma of 86
iridocyclitis with lenticular cataract 86
perithelioma 86

Fat necrosis, with gangrenous pancreatitis 211
Fenestration of pulmonary valves 156
Fischer, Martin H. 27
Fluorescent pigment, production of by bacteria 507
Folin, Otto 219
Froelich, H. 546
Frogs, epidemic, septicemic disease of 462

Gall-bladder, primary carcinoma of 175
Gall-stones, in carcinoma of gall-bladder 175
Gastro-enterostomy, spontaneous from neoplastic ulceration 276
Gehrmann, Adolph 533

Genito-urinary system 277
Giant cells, fate of, etc 486
cells, foreign body 547
Glands, ductless 89
Glioma cerebri, a case of 42
of eye 86
Glomerulitis, tuberculous 277
GRAHAM, D. W. 546
HAMILTON, ALICE 67
HARRIS, M. L. 344
Heart, aberrant tendinous cords 145
aneurism of right ventricular wall 168
congenital defect in child 174
sarcoma of parietal pericardium 158
tricuspid stenosis 174
HEKTOEN, LUDVIG 134, 172, 174, 192, 195, 205, 486
Hemangioma, simple, of upper part of small intestine 192
Hernia, internal, strangulated through a mesenteric hole .. 193
internal, strangulated through an omental slit 178
HERRICK, JAMES B. 175, 345
HERZOG, MAXIMILIAN 42, 136, 302, 317, 342, 344, 352, 432, 438, 546
Hodgkin's disease 345
HOLINGER, J. 546
Hydrochloric acid, Koeppe's theory regarding formation of in the stomach 208
Hypernephroma 283
Ileum, multiple carcinomatous constrictions with triple perforations 198
Iliac artery, arteritis with thrombosis and gangrene 174
Intestine, small, simple hemangioma of 192
Intussusception in a child 276
Iridocyclitis with lenticular cataract 86
JONES, N. W. 274, 445
JORDAN, EDWIN A. 507, 547
Keratitis, acute in the rabbit 68
Kidney, focal necroses in glomeruli 168
tuberculous glomerulitis 277
KING, H. M. 546
KLEBS, EDWIN 449
Koeppe's theory regarding the formation of hydrochloric acid in the stomach 208
Larynx, primary tuberculosis, a case of 126
LE COUNT, E. R. 89, 168, 180, 359, 546, 547
LEMKE, A. F. 49
LEWIS, HENRY F. 145
Lipoma of renal capsule 344
Lipomata 546

Liver, carcinoma, secondary 175
cirrhosis in the guinea-pig produced by a bacillus 228
hypertrophic cirrhosis in a chicken 274
sarcoma in a chicken 274
Loeb, J. 542
Lungs, metastatic abscesses 168
Lymphatic system 345
Lymphatic constitution in idiopathic epilepsy 348
Lymphoma 359
Lympho-sarcomata of mediastinum 130
sarcoma of mesentery 352
McArthur, L. L. 283
McCollum, J. L. 344
Mediastinum, lympho-sarcoma of 130
Meningitis, epidemic, cerebrospinal 67
Mergler, Marie J. 344
Mesentery, lympho-sarcoma of 352
Miller A. L. 158
Miscellany 446
Mitchell, Louis J. 89, 193
Monstrosities in the fœtus 546
Morf, Paul F. 104
Myoma of skin 432
Necroses, focal, in renal glomeruli 168
Nervous system, central 14
Neuroglioma ganglionare of brain 49
Noma in adult, complicated by amebic dysentery 180
Occlusion, congenital, in duodenum, etc 185
Ochsner, A. J. 546
Ohlmacher, A. P. 348
Osteitis deformans in a chicken 445
Ovary, adeno-carcinoma with metastasis 344
calcareous degeneration of corpus luteum cyst 302
sarcoma of 344
stones in 290
Paget's disease 438
Pancreas, hemorrhage into and about 176
Pancreatitis, gangrenous with disseminated fat necrosis .. 211
Patrick, Hugh T. 42
Patton, Joseph M. 136
Pepsin digestion; product of proteins 219
Pericardium, parietal, diffuse, small-celled sarcoma of 158
Perithelioma of eye 86
" pigmented, of eye 86
Pharynx, carcinoma of 195
Pia mater, sarcoma of 32
Placenta, early, study of in situ 317
Placentoma, malignant 311

Proteins, pepsin digestion; products of..... 219
Psammo-sarcoma of brain..... 49
Pseudoleukemia, splenic..... 364
Pulmonary conus, stenosis of..... 168
valves, fenestration of..... 156
valves, rudimentary fourth valve..... 156

Ready, C. W. F..... 174
Respiratory system..... 121
Rheumatism, etiology and treatment.....546
Rhinitis fibrinosa..... 121
Rhodes, John Edwin..... 143
Ries, Emil.....290, 303, 344, 547
Root, Eliza H..... 546
Round ligament, fibromyoma of..... 344
Russell, F. H..... 462

Salpingectomy, pathology of stump-exudates after..... 303
Sarcoma of chicken's liver..... 274
diffuse of cerebral and spinal pia mater..... 32
of parietal pericardium..... 158
showing phagocytic cells..... 546
of thyroid gland..... 104
Scarlatina, etiology of..... 525
Schaeffer, F. C..... 546
Sheldon, W. H..... 492
Sippy, B. W..... 364
Skin, the..... 411
Skin, myoma of..... 432
Spinal cord, cysticercus cellulosæ of..... 14
Spinal ganglion cell, motor, observations upon..... 27
Splenic pseudoleukemia..... 364
Stewart, J. L..... 185
Stomach, carcinoma of with retrogressive lymphatic transport..... 198
Stomach, diffuse infiltrating form of carcinoma..... 205
Stomach, Koeppe's theory of formation of hydrochloric acid in..... 208
Streptococcus pyogenes, infection with..... 168
Sudden death from pulmonary embolism..... 134
Syncytioma..... 547
Syphilis, arteriosclerosis with pancreatic hemorrhage..... 176

Thyroid gland, sarcoma of..... 104
Tubercle of brain..... 49
Tuberculosis, chronic hyperplastic of cecum..... 241
in dogs..... 492
primary, of larynx..... 126
Tumors:
Adenocarcinoma of ovary..... 344
Carcinoma of stomach, diffuse..... 205

of ileum and stomach 198
of pharynx 195
of liver 175
Fibromyoma of round ligament 344
of uterus 344
Glioma of eye 86
of brain 67
of cerebrum 42
Hypernephroma 283
Hemangioma of small intestine 192
Lipomata 546
of renal capsule 344
Lymphoma 359
Lymphosarcoma of mesentery 352
of mediastinum 130
Myoma of skin 432
Neuroglioma ganglionare of brain 49
Paget's disease 438
Placentoma, malignant 311
Perithelioma, pigmented of eye 86
Psammo-sarcoma of brain 49
Syncytioma 547
Sarcoma showing phagocytic cells 546
of ovary 344
of chicken's liver 274
of pericardium 158
of thyroid gland 104
of pia mater 32
of Wolffian body and duct 344
Uterus, fibromyoma 344
Valves, pulmonary, fenestration of 156
Van Hoosen, Bertha 546
Wagner, Carl 344
Weaver, George H. 32, 176, 228
Wells, H. Gideon 411
Wessner, John A. 208
White, Marx 277
Williams, J. C. 158
Witte, W. C. F. 198
Wolffian body and duct, tumors of 344
Yellow fever, anatomic researches in 449

RB
1
C45
v.3

Chicago Pathological Society
Transactions

Biological
& Medical
Serials

PLEASE DO NOT REMOVE
CARDS OR SLIPS FROM THIS POCKET

UNIVERSITY OF TORONTO LIBRARY

STORAGE